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Original Communications

A CONTRIBUTION TO THE BIOMECHANISM AND THE PATHOLOGY OF ECTOPIC PREGNANCY, WITH A CONSIDERATION OF SOME OF ITS CLINICAL PHENOMENA*

BASED ON A STUDY OF ONE HUNDRED AND THIRTY-ONE CASES

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MEDICAL doctrines are immeasurably influenced by the personality of the promulgator, by the medical milieu of the particular period, and by the means of research extant at the time of their formulation. It is therefore proper that scientific as well as sociologic dicta should be subjected to critical analyses and revisions from time to time, so that they may retain their value as living instruments in our realm of knowledge. Such inquiries need not always result in an overthrow of the older teachings, for they may also serve well if they bring about a clearer understanding of mooted problems, and a scientific agreement on disputed points. The subject of ectopic pregnancy furnishes an adequate illustration of this contention.

The foundation for the knowledge of extrauterine pregnancy was laid by Nelaton in 1861, when he stated for the first time, that pelvic hematocele was not a retroperitoneal hemorrhage of some unknown cause, but the end-result of a ruptured ectopic gestation. Carl Schroeder in 1866, Veit in 1884, and Voisin in 1892, have added important building stones to this chapter in gynecology. Hosts of

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pathologists and gynecologists have labored in this field since then, yet the voluminous literature on ectopic pregnancy still abounds in contradictions and uncertainties concerning some of its very fundamentals. The storm of controversy rages particularly around the following basic principles: The manner of nidation of the ectopic ovum; the formation of a reflexa; the decidual reaction of the extrauterine connective tissues; the most frequent site of rupture; the terminology defining the end-results of tubal pregnancy; and the manner and method of therapy. The material at my command has furnished me with data which throw light upon many of these mooted problems, and I offer the results of this study for consideration.

I. A DETAILED STUDY OF SPECIALLY SELECTED CASES, EACH REPRESENTING A DIFFERENT TYPE OF ECTOPIC GESTATION

CASE 1.—*Isthmial Pregnancy with an External and an Internal Rupture.* L. G. S., age twenty-six, married six years, nullipara. Menses began at the age

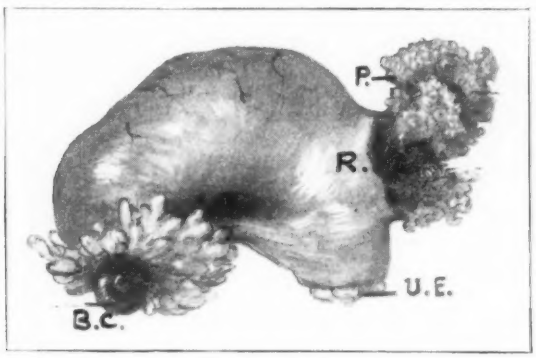

Fig. 1.—The external rupture (*R*) is filled with placental tissue (*P*), the internal rupture is indicated by the blood clot (*B.C.*) protruding from the fimbriated end. Uterine end (*U.E.*).

of twelve, twenty-eight-day type, lasting three days, moderate in amount and painless; the last period occurred on Nov. 25, 1920. On Dec. 30, 1920, she was taken ill with general abdominal pains and vaginal bleeding: the pains lasted for an hour, but the vaginal bleeding continued. On Jan. 6, 1921, she had a second attack of abdominal pain, more marked in intensity, and chiefly in the left lower quadrant of the abdomen, and radiating to the left thigh anteriorly. This attack lasted about three hours, followed by a sensation of relief, but a continuation of the vaginal bleeding. Five days later the third attack occurred, similar in character to the previous ones, and in addition nausea and fainting developed. On Jan. 19, her temperature was 100°; respiration, 28; pulse, 108, with moderate vaginal bleeding. The uterus, displaced upwards, forwards and to the right, was not enlarged; the posterior and left fornices were filled with soft doughy-like contents. Pain is elicited on displacing the cervix forwards, and on the release of abdominal pressure. A diagnosis of left tubal pregnancy was made, and a laparotomy was performed soon thereafter, which showed a ruptured isthmial pregnancy, with blood escaping through the tube wall and from the fimbriated end. The tube (Fig. 1), irregularly enlarged and distended, bluish gray in color, with a smooth

glistening peritoneal coat, showed, about 1.5 cm. from the uterine end, a rupture in its upper wall, filled with young placental tissue; its edges were bent outwards, and no other rupture point was seen. A blood clot protruded from the fimbriated end. A longitudinal section of the entire tube (Fig. 2) shows that the nidation took place in the upper wall of the isthmus, causing the latter to undergo a marked hyperplasia, with a lymphocytic infiltration and some polynucleosis, but no evidences of acute or productive inflammation. Some of the muscle fibers in this area have undergone hyaline changes. The rest of the tube wall shows marked attenuation due to the intratubal pressure, which has also caused the mucous folds to decrease in number and size. A more detailed study of the nidation site (Fig. 3) illustrates the exact formation of the capsularis and its relation to the tube lumen. A well-formed diverticulum (Figs. 4 and 5) is present in the lower wall

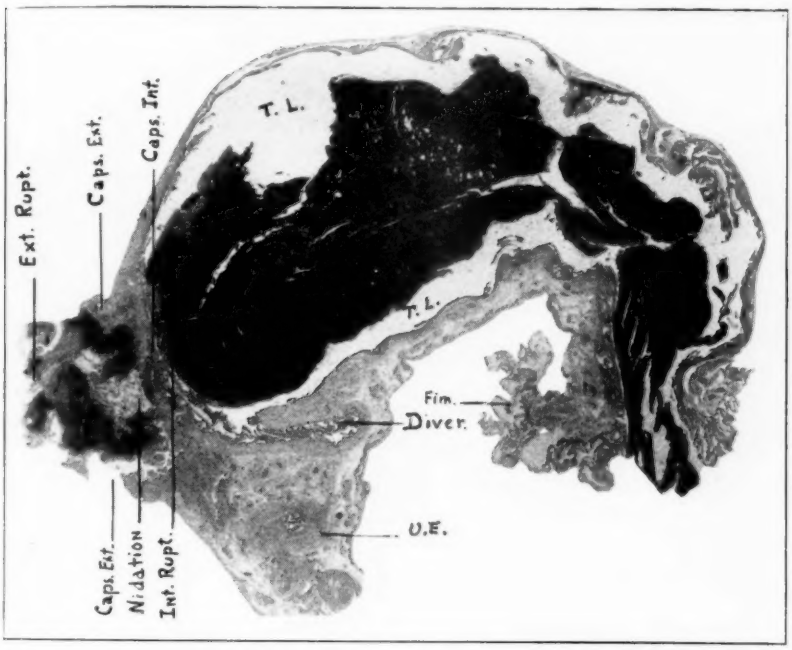

Fig. 2.—Longitudinal section of the entire fallopian tube. The nidation is in the upper wall of the isthmus. The capsularis presents a double rupture; an external (*Ext. Rupt.*) and an internal (*Int. Rupt.*). The tube lumen (*T.L.*) is filled with blood clot, which also protrudes through the fimbriated opening (*Fim.*). The diverticulum (*Diver.*) is located in the inferior wall. (*Caps. Ext.*), capsularis externa; (*U.E.*), uterine end.

of the isthmial portion, just opposite to the nidation site. This diverticulum is invested with its own muscular coats, and is lined with a mucosa identical with that of the rest of the tube. Its lumen is free, its mucosal folds not agglutinated, and it communicates freely with the main lumen. Adenomatous changes (Fig. 6) in the tube wall are found proximally to the gestation area. A well-pronounced decidual reaction is present in the walls of some of the blood vessels (Fig. 7) adjacent to the ovular bed. Under still higher magnification (Fig. 8) the decidual reaction stands out with greater clarity, against the layer of Langhans cells close to it. Epicrisis: clinically and pathologically, this case is one of isthmial pregnancy with a double rupture, one leading directly into the abdominal cavity through the capsularis externa, the other into the tube lumen through the

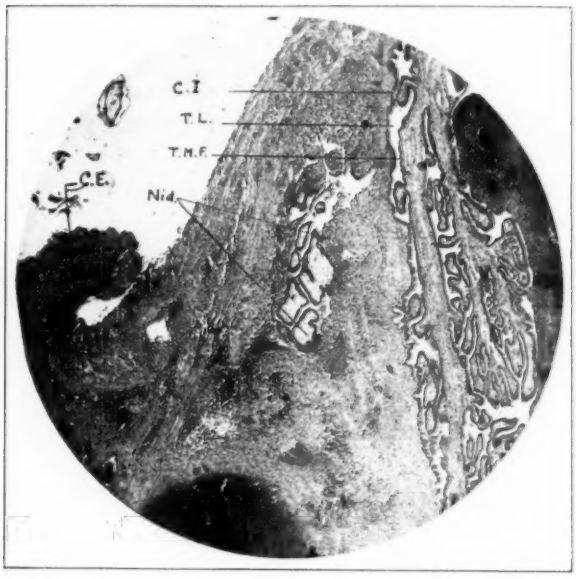

Fig. 3.—The nidation (*Nid.*) within the tube wall caused the latter to spread asunder, thus forming an outer and an inner envelope for the developing ovum. The internal capsule (*C.I.*) bears on its tubal side a covering of tubal mucosa, while the capsularis externa (*C.E.*) has a peritoneal coat. At the point of the outer break in the capsularis the edges of the rent are turned outwards. The tube lumen (*T. L.*) contains blood clot (*B.C.*). (*T.M.F.*), tubal mucosa folds.

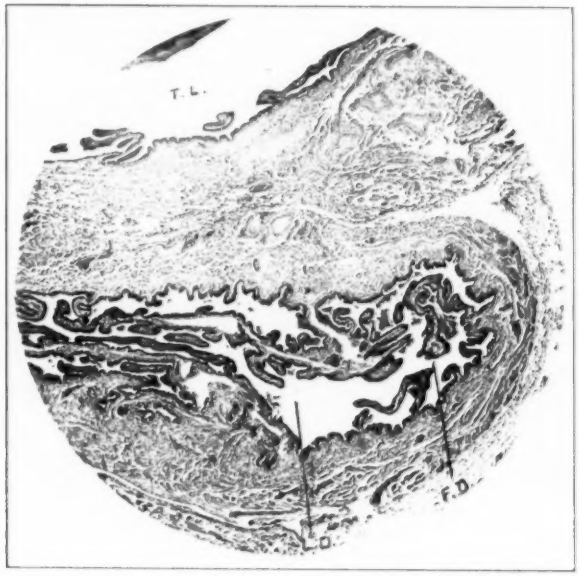

Fig. 4.—Tubal diverticulum showing the fundus of diverticulum (*F.D.*), and part of the lumen (*L.D.*). The tube lumen (*T.L.*) is above.

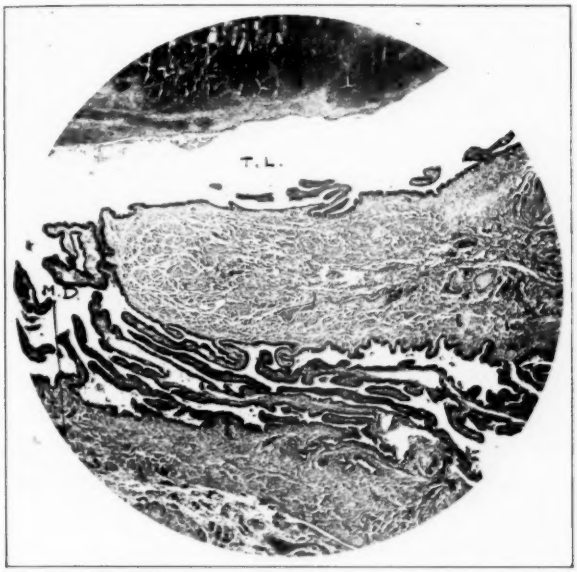

Fig. 5.—Tubal diverticulum, terminal portion. The mouth of diverticulum (*M.D.*) joining the tube lumen (*T.L.*).

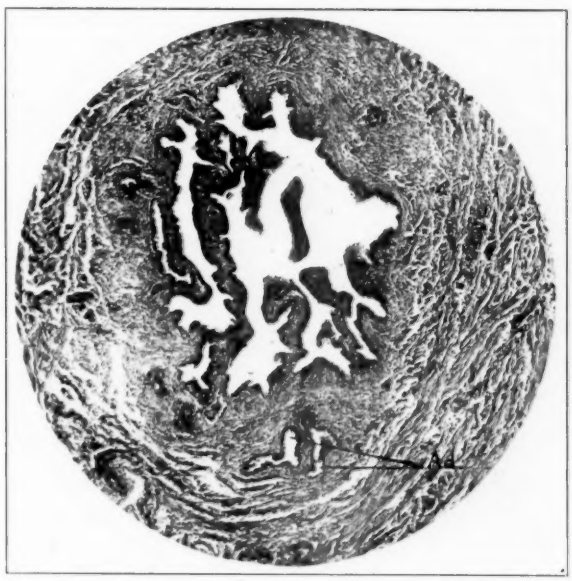

Fig. 6.—Isthmial portion of the tube proximal to point of nidation, showing adenomyomatous changes (*Ad.*) in the wall.

internal capsule, from where the blood gained access to the peritoneal cavity through the fimbriated opening. From the manner in which the edges of the rent in the external capsule are bent it may be inferred that two forces were active in the production of the rupture: (a) a hemodynamic force, resulting from

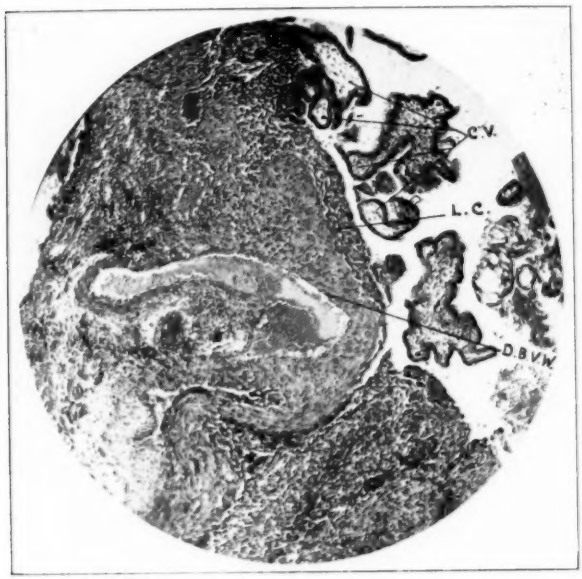

Fig. 7.—Decidual reaction in a blood vessel wall (*D.B.V.W.*). A layer of Langhans' cells (*L.C.*) stands out in marked contrast to the decidual reaction in the wall of the blood vessel on one side, and to the chorionic villi (*C.V.*) on the other.

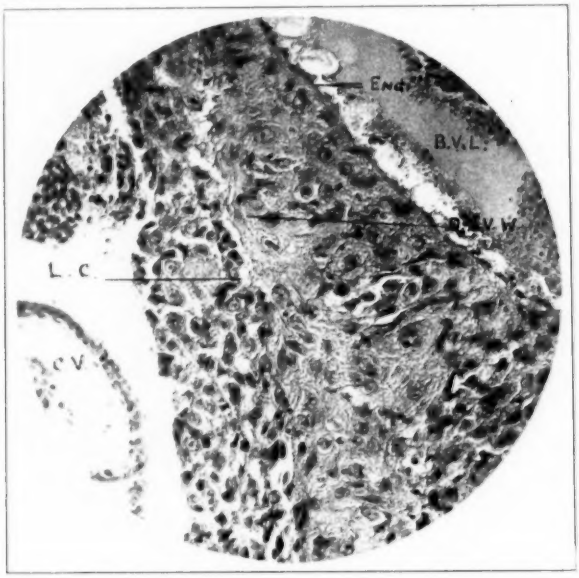

Fig. 8.—A still higher magnification of the decidual reaction in the blood vessel wall (*D.B.V.W.*), showing the blood vessel lumen (*B.V.L.*), the endothelial lining (*End.*), the layer of Langhans' cells (*L.C.*), and part of a chorionic villus (*C.V.*).

the excessive intracapsular hemorrhage, which tore the already weakened and eroded wall, and (b) a myodynamic force, exerted by the intact muscle fibers upon the damaged ones, pulling the latter apart. The internal rupture is proved by the

large quantity of free blood in the tube lumen. The diverticulum in this case I consider as congenital for it is invested with its own muscular coats, thus differing from the endosalpingial invasion of the muscularis as a result of suppurative salpingitis. It is also noteworthy that the diverticulum, although of large size and communicating freely with the main tubal lumen, did not trap the migrating ovum.

CASE 2.—*Isthmial Pregnancy with an Intracapsular Rupture.* E. A., age twenty-six, one child, two years and eight months ago; two spontaneous miscarriages, one, three and a half years ago, and the second, eight months ago. Menses began at the age of thirteen, twenty-eight-day type, lasting three days, painless and moderate in amount. The last period occurred on Jan. 21, 1921. On Feb. 3, after bathing, she noticed some vaginal staining, accompanied by pain in the left lower quadrant of the abdomen, which radiated to the left thigh anteriorly. On Feb. 27, the abdominal pain became more intense and the vaginal bleeding more profuse. On the following day she felt a sudden gush of watery fluid from the vagina and the expulsion of a few blood clots (most likely a decidual cast). A physical examination on March 7, 1921, showed a slightly irregular but not enlarged or softened uterus. The right adnexa were palpable and apparently normal. To the left of

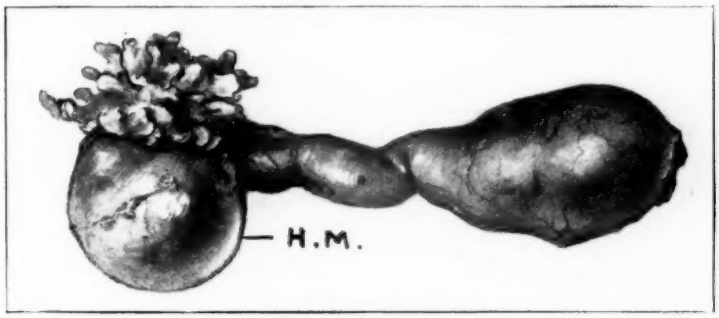

Fig. 9.—The superficial blood vessels show congestion, and at the fimbriated end an hydatid of Morgagni (*H.M.*) is attached.

the uterus and close to it, appeared a fusiform tumor mass, separate and distinct from the ovary, and from another round cystic tumor the size of a walnut, anteriorly. The vaginal fornices were free. Diagnosis: left tubal pregnancy unruptured. Operation, performed April 19, 1921, consisted of a left salpingectomy and appendectomy; no free blood in the peritoneal cavity.

The specimen (Fig. 9) consists of the fallopian tube (viewed from behind), irregular in outline due to a pear-shaped enlargement of its inner half, which is marked off from the nondilated portion by a twist in its long axis. The peritoneal surface is smooth and glistening and the superficial blood vessels congested. An hydatid of Morgagni the size of a walnut is attached to the lower free border of the fimbriated end. A longitudinal section of the entire tube (Fig. 10) shows the pregnancy to be located in the inner half of the tube, which is distended to its outmost capacity. The gestation mass consists of a large blood clot, chorionic villi, fibrin, clumps of syncytium and débris. The lacunar hemorrhage stayed within the capsular confines, distended and pushed it towards the surrounding tube wall, with which it fused into one structure, thus obliterating the landmarks of the reflexa. In or about the center of the gestation mass the embryonic vesicle is seen, consisting of a hyaline homogeneous pinkish staining mass, surrounded by the amnion with its outer chorionic envelop; no traces of the embryo are found. The

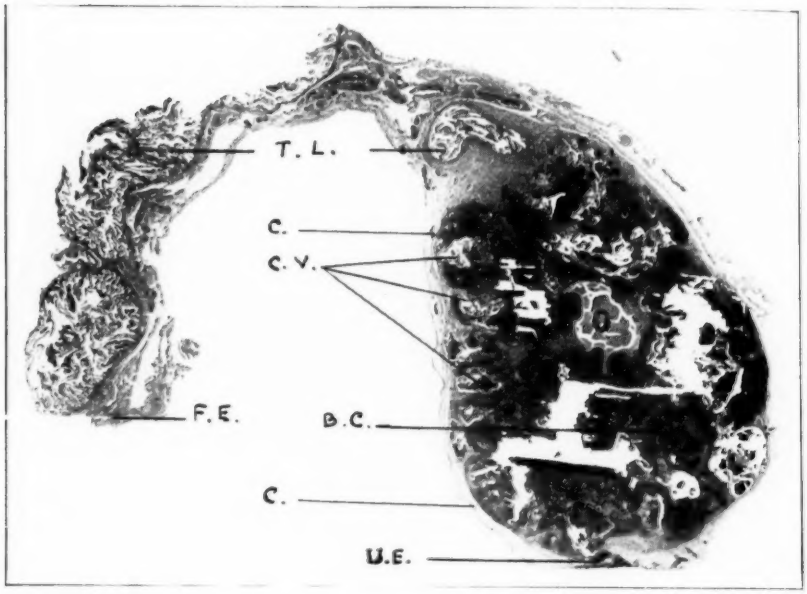

Fig. 10.—Longitudinal section of the entire tube. The gestation mass occupies the isthmial half; it consists of blood clot (*B.C.*); chorionic villi (*C.V.*), the remains of the ovum (*O*), and débris. It is surrounded by the thinned out but intact tube wall, which forms the capsularis (*C.*), so that the hemorrhage remained within its confines. The uterine and the fimbriated ends are seen respectively at (*U.E.*) and (*F.E.*). The tube lumen (*T.L.*) was displaced to one side.

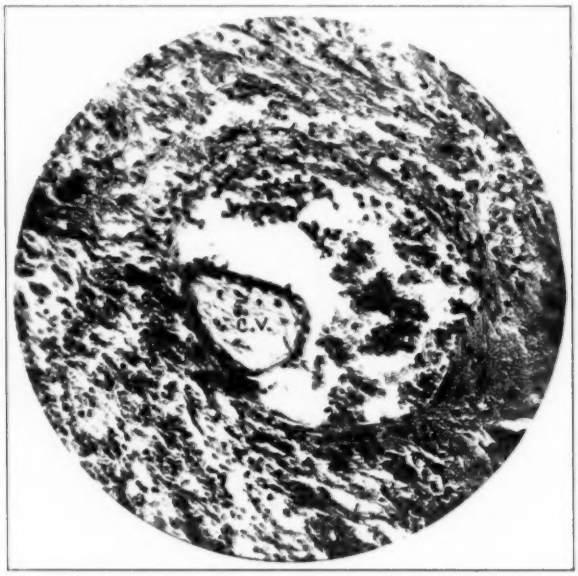

Fig. 11.—Cross-section of a vein containing a chorionic villus (*C.V.*).

tube lumen is pushed over to one side, and it presents a normal appearance. The stasis in the superficial blood vessels is due not only to the pressure by the intratubal contents, but also and chiefly to the obstruction of many of the venous channels by trophoblastic masses within their lumina (Fig. 11). Epicrisis: This case is one of intracapsular rupture, clinically considered as an unruptured tubal gestation, because no blood escaped either through a rent in the tube wall or through the fimbriated end. It is also of great interest to note the fact that, according to the statement of the patient, no menstrual period was skipped, and the uterine bleeding manifested itself as early as the thirteenth day after the last period. From these data it may be inferred that while the ovular death was signaled by the first appearance of the uterine bleeding, the extensive intracapsular bleeding has continued for some time thereafter, through the posthumous activity of the chorionic villi.

CASE 3.—*Ampullar Pregnancy with Multiple External Ruptures.* I. E., age thirty-nine, married sixteen years, has had three children, the last one thirteen

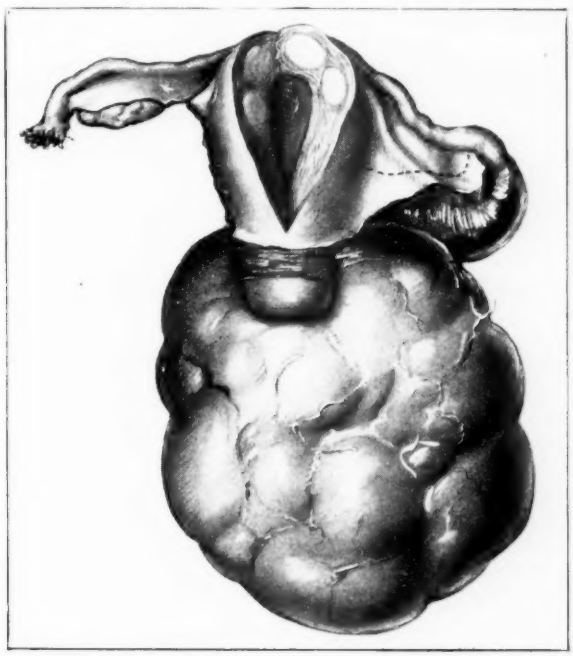

Fig. 12.—Ampullar pregnancy with multiple arrosions, and complicated by fibroids of the uterus, interstitial and subserous in type.

years ago, and three induced abortions, the last one eight years ago. Menses began at the age of fourteen, twenty-eight-day type, lasting five to six days, moderate and painless; the last period occurred on April 18, 1921. On June 1, 1921, she noticed some vaginal staining which lasted for a few hours; six days later there was a return of the bleeding for one day. On June 9, at three A.M., sudden sharp pains were felt in the hypogastrium, radiating to the rectum; these pains recurred at irregular intervals with increasing severity, and accompanied by fainting sensations. For the past few days she also complained of dyschesia, and with each attack of pain the vaginal bleeding increased. Physical examination, June

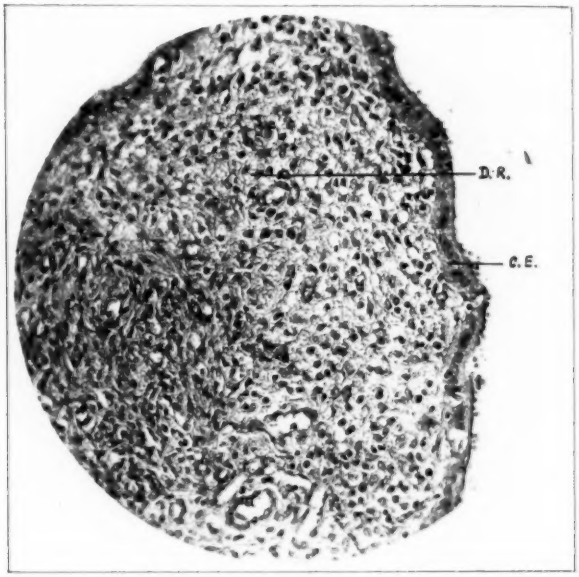

Fig. 13.—The submucosa of the isthmial part of the tube showing a pronounced decidual reaction (*D.R.*). The overlying columnar epithelium (*C.E.*) has a normal appearance.

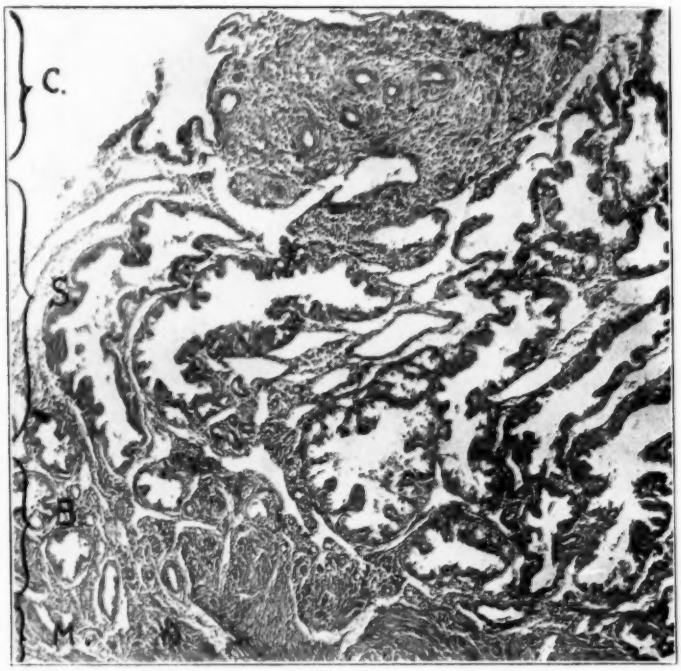

Fig. 14.—Uterine mucosa in tubal pregnancy, presenting all the hyperplastic changes characteristic of pregnancy, excepting the presence of trophoblastic elements. (*C.*) Compacta; (*S.*) Spongiosa; (*B.*) Basalis; (*M.*) Muscularis.

20, showed abdomen tender to touch over the lower half, and dull on percussion. A vaginal discharge of dark fluid blood was present. The uterus was enlarged to the size of a two months' gestation, irregular in outline due to several interstitial fibroids, and displaced upwards and to the right by a hard pelvic tumor, the size of a grapefruit. To the left of the pelvic tumor was a fluctuating area. Diagnosis: ruptured tubal pregnancy and uterine fibroids. Operation June 20, consisted of an abdominal panhysterectomy and the evacuation of free and clotted blood from the peritoneal cavity. The uterus contained several interstitial fibroids in the fundal portion, and together with its adnexa was perched upon a large infracervical subserous fibromyoma (Fig. 12). The left tube was very much lengthened, distended in its outer half to the thickness of an index finger, purple in color and adherent to the posterior surface of the uterus and the broad ligament. The dilated portion of the left tube harbored a clotted bloody mass containing chorionic villi, fibrin, free trophoblastic islands and débris. The capsularis was made up of the attenuated tube wall, whose musculature was reduced to but a few isolated fibers, the mucous folds hardly recognizable, and the serous coat riddled with many perforations and erosions. No reflexa could be identified, nor could any decidual reaction be noted within or immediately near the gestation area, but in the submucosa of the isthmial portion a pronounced decidual reaction was present (Fig. 13). The uterine mucosa (Fig. 14) presents the characteristic morphology of a decidua of pregnancy. Epicrisis: This case represents an ampullar pregnancy, in an adherent tube with multiple external ruptures, many of which were closed by chorionic villi. This is the reason that the internal bleeding in these types of pregnancy is insidious and why they are operated upon much later than the acute forms. Due also to the late date of the operative procedure, the finer anatomic structures of early pregnancy are no longer discernible.

CASE 4.—*Ampullar Pregnancy with Intermo-External Rupture.* A. J., age thirty-three, married sixteen years, one child fifteen years ago, and one induced abortion eight years ago. Was operated upon for a right-sided tubal pregnancy four years ago. Menses began at the age of thirteen, twenty-eight-day type, lasting two days, scanty and painful; the last period occurred July 17, 1918. After an amenorrhea of six weeks, the patient was seized with sharp cramp-like pains in the lower abdomen accompanied by vaginal bleeding. The family physician considered the condition as an incomplete abortion and curetted. As this procedure did not alleviate her pains or stop the bleeding a consultation was requested. My examination on Sept. 2, 1918, revealed a pale looking woman with an irregular pulse varying in frequency from 96 to 110, respiration 28, and temperature 104° F. To the left and posterior to the uterus a fixed fluctuating mass was found. A diagnosis of a ruptured tubal pregnancy was made and an immediate operation performed, consisting of a left salpingo-oophorectomy and removal of the blood clots from the pelvis. No drainage was employed, and the recovery was uneventful. The fallopian tube was dark red and irregular in outline due to two bulbous enlargements, each about the size of a plum. The peritoneal surface was rough, and there were two perforations, one 2 cm. from the fimbriated end, and another one about the middle of the tube. A blood clot was also protruding from the fimbriated end. The isthmial portion (Fig. 15) presents throughout its entire length a double lumen, up to the gestation site, each of which has its individual layers of muscle, but only one serous and subserous coat envelops both of them. The mucosa in both lumina showed unmistakable evidences of a chronic salpingitis (Fig. 16), yet the columnar epithelium was well retained, and in many places also the ciliary covering. A moderate quantity of free blood was present in the tubal lumen. The submucosa showed a mild infiltration with round cells and a moderate decidual reaction. Some of the sections

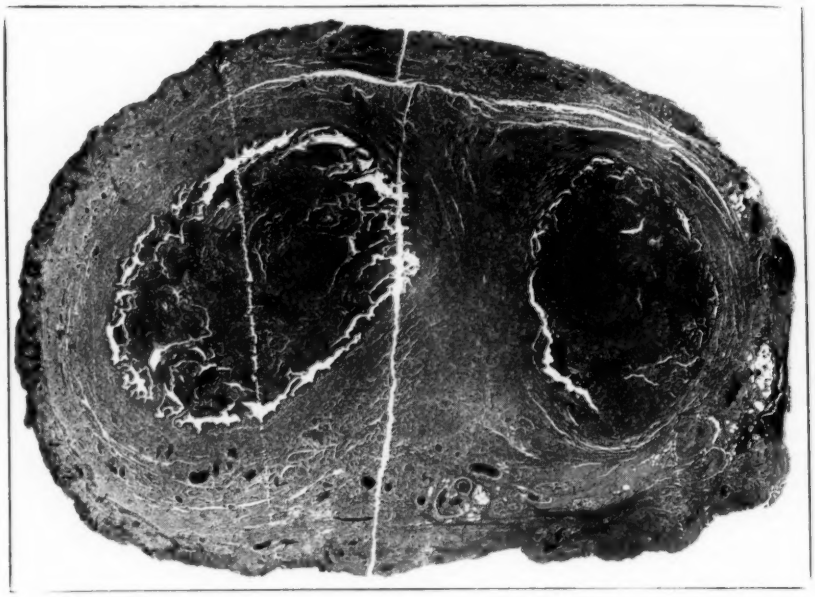

Fig. 15.—The isthmial portion of the tube presenting a double lumen, each surrounded by a definite internal circular and an outer longitudinal muscle layer, but with a single serous and subserous envelope.

Fig. 16.—A high power study of the isthmial portion of the tube, showing a well advanced chronic inflammation, a mild decidual reaction in the submucosa, no agglutination of the mucous folds, a retention of the columnar epithelium and in many parts also of the ciliated covering. A moderate quantity of free blood present in the tube lumen.

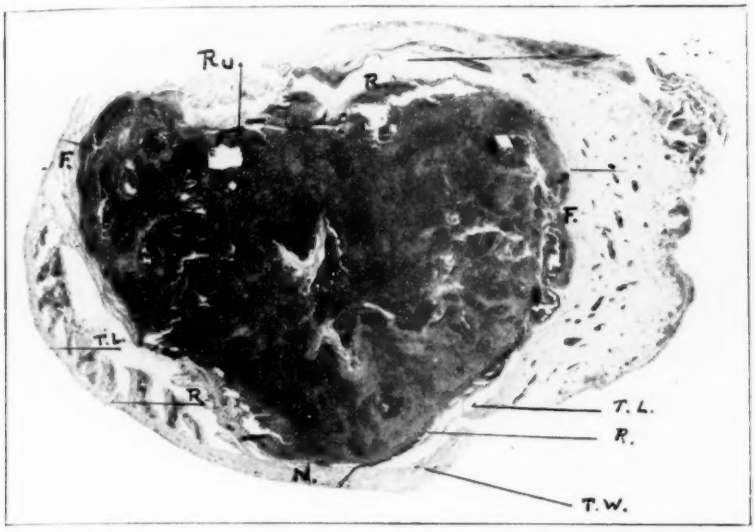

Fig. 17.—The nidation (*N*) is mucosal in type. The reflexa (*R*) surrounds the gestation mass which developed centripetally. At a point directly opposite the placentation area, fusion (*F*) between the reflexa and the tube wall occurred and at this point the rupture (*Ru.*) took place. The tube wall (*T.W.*) at the site of nidation has not been invaded by the trophoblast, and the tube lumen (*T.L.*) is seen to either side of the reflexa.

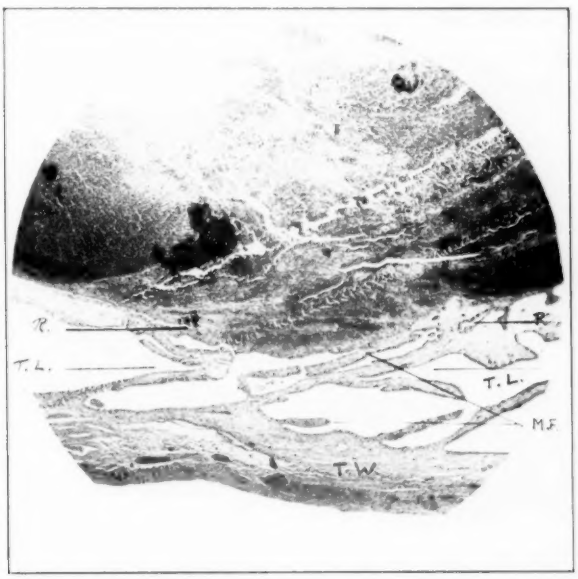

Fig. 18.—A more detailed study of the mucosal type of nidation. The beginning of the reflexa (*R*) is seen to either side of the ovular attachment, the latter resting upon the mucous folds (*M.F.*). The tube lumen (*T.L.*) is free, and the tube wall (*T.W.*) while thickened, is not encroached upon by any products of gestation. *T.W.*, tube wall.

also showed adenomatous proliferation. The nidation (Fig. 17) is mucosal in type, the latter forming a distinct reflexa which fused with the opposite wall of the tube. The rupture took place at the point of fusion. The tube wall directly under the

placentation site (Fig. 18) showed a marked hyperplasia, a round-cell infiltration, an engorgement of its blood vessels, but no trophoblastic invasion. Epicrisis: In this case we find biomechanical factors identical with those seen in intrauterine gestation; namely, a mucosal nidation, and a distinct reflexa. Contrary to the prevalent teaching, the rupture took place at a point opposite the placentation site; this observation is not at all uncommon in my experience. The type of rupture is an interno-external form. By this I mean that the internal capsule had to be eroded before the outer wall of the tube, through which the break has finally occurred. Evidences of chronic inflammation were present in the submucosa of the isthmial portion, while in the ampullar part which harbored the pregnancy they were lacking. Furthermore, the columnar epithelium and its ciliary covering were well retained throughout the greater portion of the tube. It is therefore possible to state with positiveness that in this case at least, neither mucosal folds, nor the want of cilia were responsible for the extrauterine nidation of the ovum. Whether the double tube seen in the proximal portion is a congenital condition or an artifact occasionally encountered in sections of chronic salpingitis, is a debatable question. While I am inclined to an inflammatory genesis, the uniformity and singleness of the serous coat, and the separate muscular coats of each lumen speak in favor of a congenital derivation. Cases of double tubes have been described by Keppler, Schantz and others, some of these authorities attempted to explain the absence of the double lumen in the ampullar portion, as seen in my case, on the basis of a postnatal involution. It requires an unusual stretch of the imagination to fit this theory into the framework of embryologic reasoning.

CASE 5.—*Ampullar Pregnancy with an Interno-External Rupture.* C. K., age twenty-three, married two years, nullipara. Menses began at the age of thirteen, twenty-eight-day type, lasting three to four days, normal in amount and painless; the last period occurred on Feb. 2, 1924. On March 17, she began to spot, one week later she felt a sharp sticking pain in the lower quadrant of the abdomen which radiated to the rectum. These symptoms lasted for one day. On April 1, 1924, she was admitted to the hospital complaining of pain in the lower abdomen, and the left shoulder, and of a fainting sensation. Physical examination showed a tense lower abdomen, dull to percussion and tender on the release of pressure. The cervix, somewhat softened, pointed to the left and the uterus was displaced upwards and to the right. The posterior and both lateral fornices were full. Blood count: R. B. C. 2,750,000; W. B. C. 13,000; polys., 84 per cent; lymph., 16 per cent. Diagnosis: ruptured tubal pregnancy. Operation performed soon after admission consisted of a right salpingectomy, appendectomy, and the evacuation of the free blood from the peritoneal cavity. The right fallopian tube (Fig. 19), irregularly enlarged in its outer two-thirds, was bent upon itself in an inward and downward direction. The distended, ampullar portion was bluish in color and measured 3.75 cm. at its widest diameter. The peritoneal coat was smooth and glistening, and at a point 1 cm. from the fimbriated end, the continuity of the tube wall was broken. This rent was filled with young placental tissue; the fimbriated end was patent and its lumen was free. The isthmial uninvolved portion was normal and its lumen empty. The nidation was in the inferior wall (Fig. 20) and as the pregnancy developed in an inward direction, it displaced the tube lumen to one side. Due to this form of ovular growth the internal capsule was gradually raised, thus forming a true reflexa and with the still further development of the pregnancy, the reflexa was finally brought into intimate contact with the opposite wall of the tube with which it fused. The rupture took place at this point of fusion. Besides the main rupture, smaller eroded but closed areas were present in the tube wall at the site of placentation, one of these is reproduced more minutely in Fig. 21. A detailed

study of the reflexa (Fig. 22) shows that it is composed of the following structures: The central massive part is chiefly muscular derived from that part of the tube wall which lay above the ovum, it is infiltrated with round cells, some of

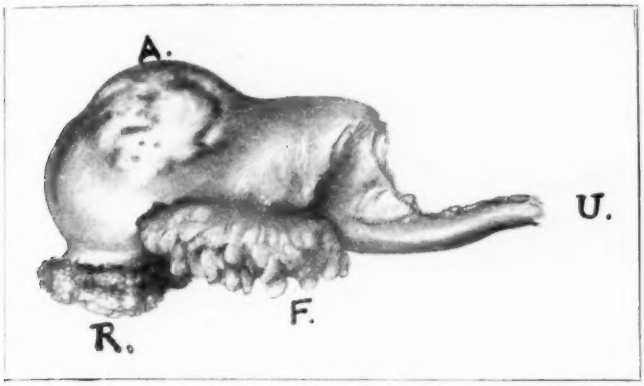

Fig. 19.—Ampullar pregnancy with an interno-external rupture, and a closed arrosion. Uterine end (*U*), fimbriated end (*F*), rupture (*R*), and arrosion (*A*), which is closed.

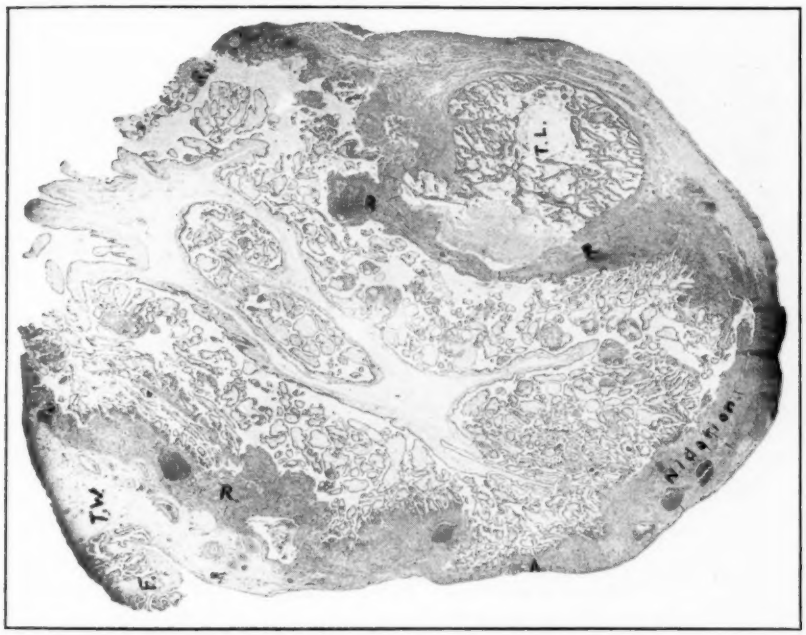

Fig. 20.—Cross-section through the ruptured area. The nidation is intramural and the development of the ovum progressed centripetally, thus forming a reflexa of the inner part of the tube wall (*R*). The rupture (*Ru.*) took place through the internal capsule and the opposite tube wall (*T.W.*) simultaneously. The tube lumen (*T.L.*) is seen displaced to one side. At (*A*) an arrosion is seen which is plugged with chorionic villi.

the fibers show hyaline changes due to the lytic action of the trophoblast, and some edema. The intermuscular connective tissue shows a decidual reaction, and it is most pronounced in the walls of some of the blood vessels. On the fetal surface

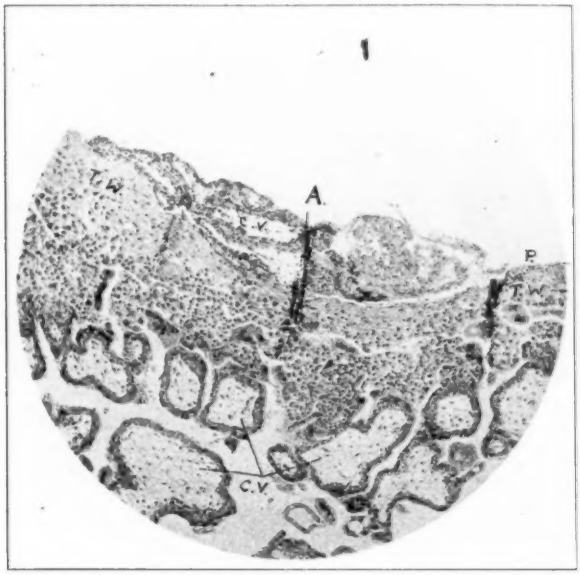

Fig. 21.—A high power study of an arrosion (*A*) which is closed with the products of gestation. The tube wall (*T.W.*) is invaded with Langhans' cells and syncytium, and its peritoneal coat (*P*) is seen on the left. (*C.V.*) chorionic villi.

Fig. 22.—The reflexa (*R*) in more magnified view. The tube lumen (*T.L.*) contains some débris and old blood. On the fetal side the reflexa is in contact with Langhans' cells (*L.C.*), chorionic villi (*C.V.*), and masses of syncytium (*Syn.*), and on the maternal side it is covered with tubal mucosa (*T.M.*).

the reflexa is covered with a layer of fibrin, and products of gestation, and on the maternal side with the tubal mucosa. The placental site (Fig. 23) is denoted by the securer anchorage of the chorionic villi, the pronounced hyperplasia of the

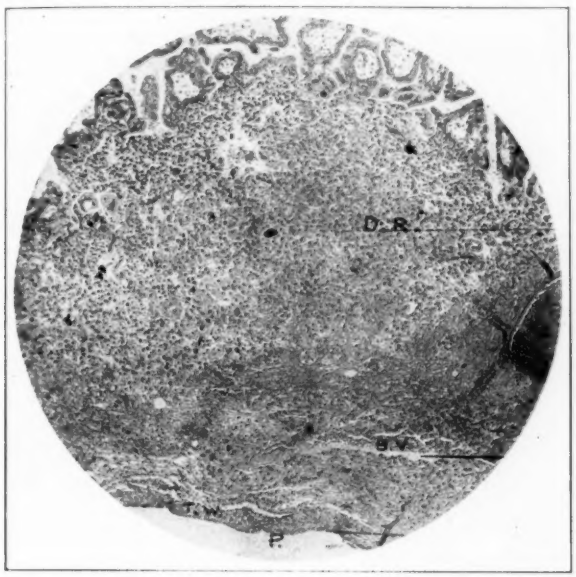

Fig. 23.—The nidation area highly magnified. It shows the hyperplasia of the tube wall (*T.W.*), with a pronounced decidual reaction (*D.R.*), the latter extending also to the walls of the blood vessels (*B.V.*). The peritoneal coat (*P*) is normal.

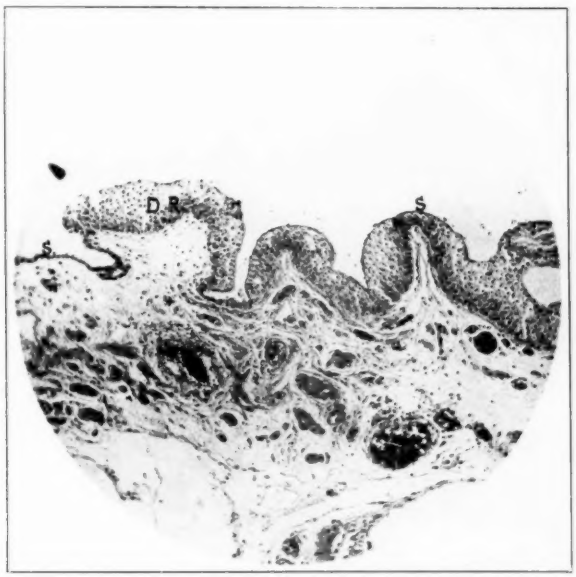

Fig. 24.—The isthmial nongravid part of the fallopian tube, presenting a very pronounced decidual reaction (*D.R.*) in the subserosa. The serous (*S*) covering is normal.

tube wall, the very marked decidual reaction and by the anatomic origin of the reflexa to either side of the ovular bed. Besides the decidual reaction within and adjacent to the gestation area, more remotely lying connective tissue elements

have also responded proliferatively to the hormones of pregnancy; such a response is found in the subserosa of the isthmial portion (Fig. 24). Epicrisis: The type of rupture in this instance is interno-external, shown by the absolute freedom of the tube lumen from any blood or gestation elements, and by the erosion of the capsularis interna and then of the overlying tube wall. Here again the rupture occurred opposite the placental attachment. The only suggestion of a previous salpingitis is the network formation of the mucosal folds seen in the uninvolved portion of the tube. This assumption was strengthened later on through a subsequent inflation test of the remaining tube, which proved to be closed.

CASES 6 AND 7.—*Successive Tubal Pregnancies with Internal Ruptures.* B. P., married two and a half years, nullipara; miscarried once seven months ago in the eighth week of pregnancy. Menses began at the age of fourteen, thirty-day type, lasting three to five days, painless and moderate in amount; the last period occurred

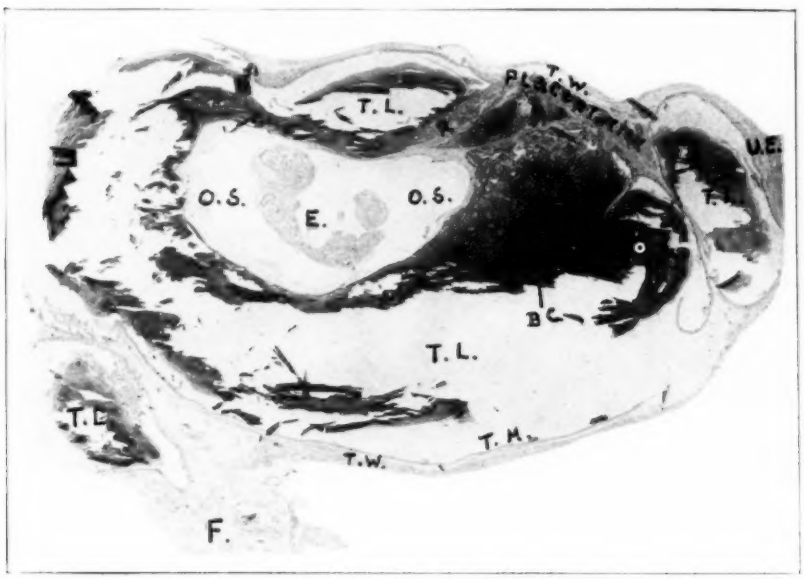

Fig. 25.—Longitudinal section of the left gravid tube. The placentation is in the upper wall of the isthmial portion. The gestation consisting of the embryo (*E.*) surrounded by the ovular sac (*O.S.*), and the overlying tubal mucosa and part of the tube wall, which formed respectively a reflexa (*R*) and a capsularis has developed in an inward direction. The outer layers of the capsularis are broken and the escaping blood from the lacunar spaces fills the tube lumen (*T.L.*) from the uterine (*U.E.*) to the fimbriated (*F*) end. At the area of placentation the tube wall (*T.W.*) showed thickening while in the rest of its extent, thinning. Blood clot (*B.C.*). Tubal mucosa (*T.M.*).

Feb. 14, 1921. On March 22, sudden pain in the left lower quadrant of the abdomen, cutting in character, followed soon by vaginal bleeding. On March 27, two fainting spells, and on April 5, another one. Physical examination on April 10, showed a pale looking woman of normal stature and development, the lower abdomen tender to touch particularly on the release of pressure. Vaginally—dark fluid blood escaped freely, the uterus was dextroverted, tender to manipulation, globular in outline, and not enlarged. A sensitive elongated tumor mass the width of two fingers occupied the left fornix, and part of the cubdesac of Douglas. Diagnosis: ruptured tubal pregnancy. An immediate operation was performed: the left tube removed and the peritoneal blood evacuated. The left fallopian tube was irregularly enlarged into a

conical bluish tumor, the widest diameter at the outer end; the abdominal ostium was filled with blood clot. The peritoneal coat was smooth, no adhesions, and the superficial blood vessels markedly congested. The dilated portion of the tube contained an embryo (Fig. 25) 65 mm. in length, surrounded by the ovular sac, and the nidation was in the upper wall of the isthmial portion at a point 1 cm. from the uterine end. The embryo developed towards the tube lumen and the rupture occurred in the internal capsule opposite the nidation area. The tubal mucosa was normal, the lumen to either side of the gestation site patent and contained blood. A distinct reflexa (Fig. 26) surrounded the gestation mass, composed of muscle fibers, infiltrated with round cells, and the interstitial connective tissue showed a decidual reaction. On the fetal side the reflexa was covered with fibrin and trophoblastic elements, and on the maternal surface with tubal mucosa. On Dec. 7, 1924, this same patient telephoned to me that she was again ill with a tubal pregnancy.

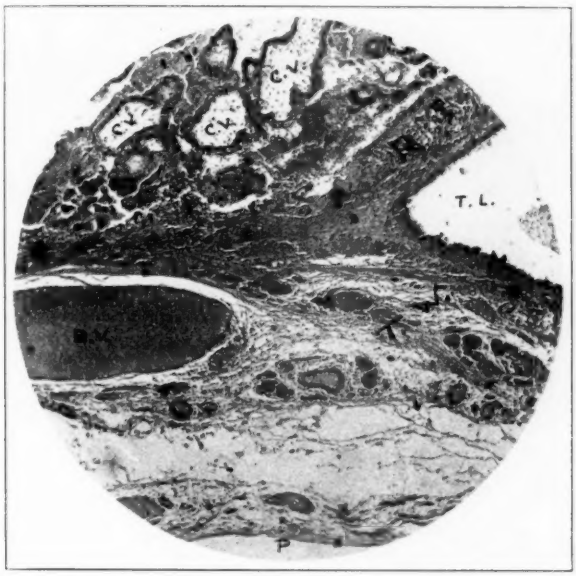

Fig. 26.—High power microphotograph of part of the nidation area, showing the hyperplasia of the tube wall (*T.W.*), with the marked engorgement of its blood vessels (*B. V.*). The reflexa (*R.*) consists of the inner portion of the tube wall which was lifted up by the growing gestation mass, which lies outside the tube lumen (*T.L.*); the decidual reaction (*D.R.*) within the reflexa is very pronounced; (*M.*) mucosa of tube; (*P.*) peritoneal surface; (*C.V.*) chorionic villi.

I ordered her to the hospital at once, and on admission she gave the following history: Since her operation in 1921, her menses continued regularly, the last period occurred on Oct. 22, 1924. On Dec. 3, she began to stain; this lasted for a few hours only. Two days later sudden severe pains in the right iliac fossa, and fainting. A physical examination corroborated the patient's diagnosis of a right sided tubal pregnancy. A laparotomy was performed soon after the examination and the right tube removed. It measured 5 by 1 cm., was irregularly enlarged into two nodular swellings, color was dark blue, and the peritoneal surface smooth, glistening, and intact. Blood clot protruded from both ends of the tube. On cross section (Fig. 27) the nidation showed an intramural character involving the isthmial portion. The ovular development progressed towards the tube lumen, thus evolving a well-formed reflexa. The rupture took place in the internal capsule with the blood

from the lacunar spaces escaping into the tube lumen. Besides the chorionic villi, the masses of trophoblast, the fibrin, and the blood, constituting the gestation mass, and part of the amniotic cavity were also present. The tube wall was thickened throughout its entire course and in the ampullary part presented adenomyomatous formations. Epicrisis: The macroscopic or clinical diagnosis usually made in such instances is one of tubal abortion, since the fimbriated opening was the only avenue through which the gestation products found their way to the peritoneal cavity. The microscopic investigation, however, proved that we were dealing with a rupture of the internal capsule in both instances. It is also worthy of notice, that each time the rupture was opposite to the placental site. Marked decidual reaction within the gestation area was also present in each specimen.

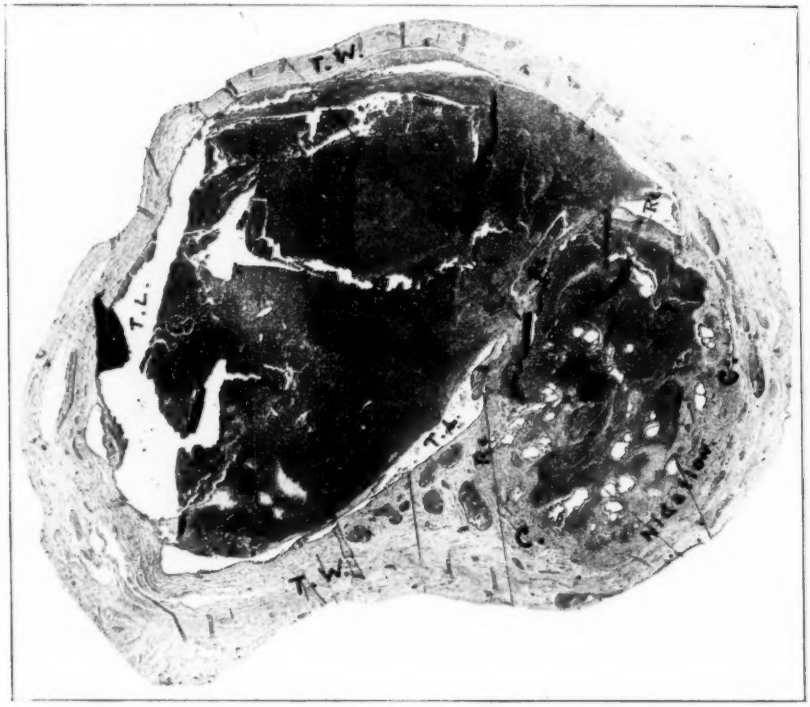

Fig. 27.—Cross-section of the isthmial portion of the right gravid tube. The gestation is intramural in character involving the inferior tube wall (*T.W.*) which shows a marked thickening throughout its entire circumference. The inner part of the tube wall forms the capsularis (*C*), and the mucosa, the reflexa (*Re.*). The rupture (*R*) point is in the internal capsule through which gestation products gained access into the main lumen of the tube (*T.L.*).

Case 8.—*Interstitial Pregnancy with Intracapsular Rupture.* A. H., aged thirty-eight, married fifteen years, para i fourteen years ago, one miscarriage twelve years ago, remained sterile since then. Menses began at the age of seventeen, twenty-eight-day type, four days' duration, moderate in amount and painful, the last period occurred Oct. 20, 1924. Early in December she began to feel nauseated; one week thereafter she was taken ill with intermittent cramp-like pains in the lower abdomen and in the back. A physical examination on Dec. 28, revealed the following facts: General condition good, vaginal mucosa of a purplish hue, no bleeding, the cervix displaced and pressed upwards against the symphysis pubis. The uterus

was dislodged upwards and backwards to the left, by a hard nodular tumor in the hollow of the sacrum. The uterine adnexa were not palpable. A diagnosis of intrauterine gestation complicated by fibroids was made. On Dec. 31, 1924, I performed a laparotomy and found the following conditions: The body of the uterus slightly enlarged was rotated on its long axis to an angle of 90° from left to right, and perched upon a hard nodular tumor which occupied the posterior pelvic fossa. It proved to be a pedunculated subserous fibromyoma, the size of a large adult fist, springing from the upper and anterior surfaces of the body of the uterus. The adnexa were normal in appearance. A panhysterectomy was performed, there was no free blood in the peritoneal cavity. The specimen (Fig. 28) included a subserous fibromyoma projecting from the anterior surface of the fundus. The right uterine

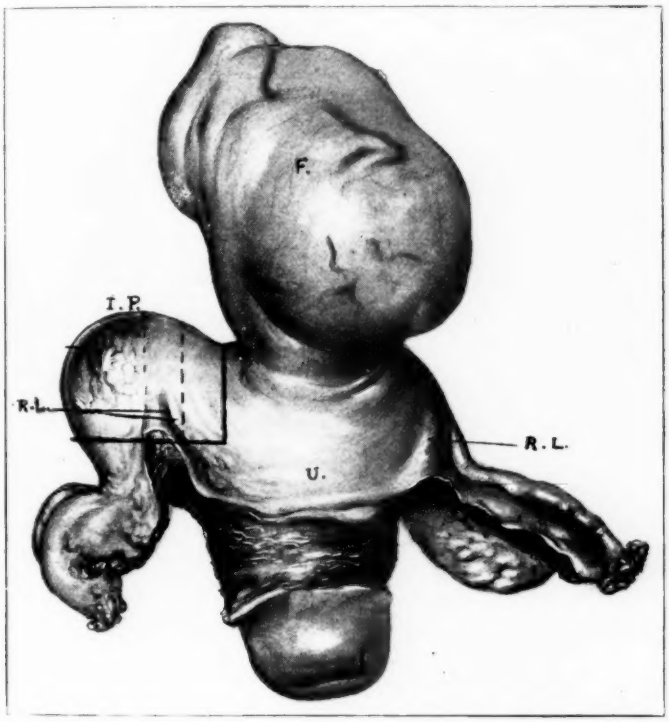

Fig. 28.—Right interstitial pregnancy (*I.P.*) with an intracapsular rupture. Note the origin of the round ligaments (*R.L.*), the one on the right is below, in front, and to the inner side of the gestation mass. The fibroid (*F*) springs from the anterior surface of the fundus uteri (*U*).

cornu presented a globular smooth swelling, which was of a softer consistency than the rest of the uterus, and with marked engorgment of its superficial blood vessels. The origin of the round ligament on the right side was on the same level as the one on the left, and lay in front, below, and proximally to this mass. The part of the specimen indicated by the heavy lines in Fig. 28 was resected hardened and cut, in an anteroposterior direction into numerous sections, the findings were as follows: The interior of the tumor was hollow, the inner surface of this cavity was wavy, glistening, and grayish in color, covered by a fine membrane composed of the chorion and the amnion. No traces of the embryo were found, apparently lost in the process of fixation. The capsularis contained a moderate amount of blood, the chorionic

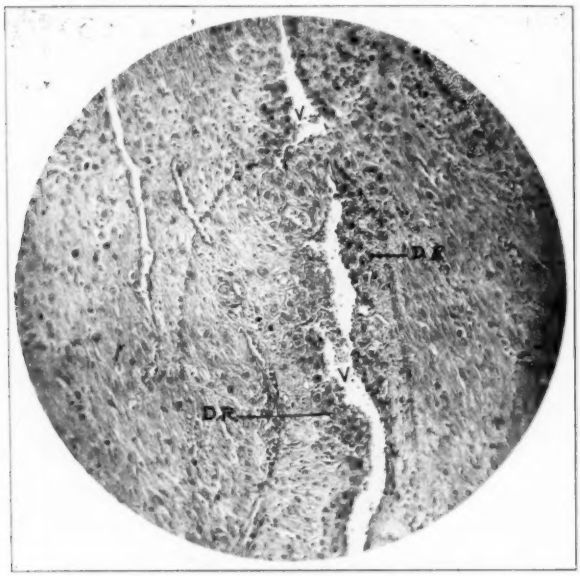

Fig. 29.—Longitudinal section of a vein (*V*), with a marked decidual reaction (*D.R.*) in its walls.

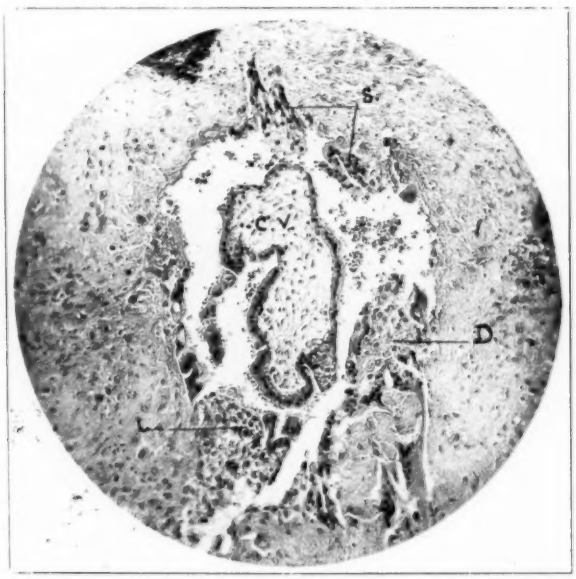

Fig. 30.—Blood vessels containing chorionic villi (*C.V.*), syncytium (*S*), Langhans' cells (*L*), and a decidual reaction (*D*) in its wall.

villi presented a normal appearance and merged imperceptibly and irregularly into the surrounding uterine musculature. The adjacent muscle fibers were split up by the invading chorionic villi into irregular strands and spaces, and many of them showed hyaline changes. The intermuscular connective tissue of this area showed a

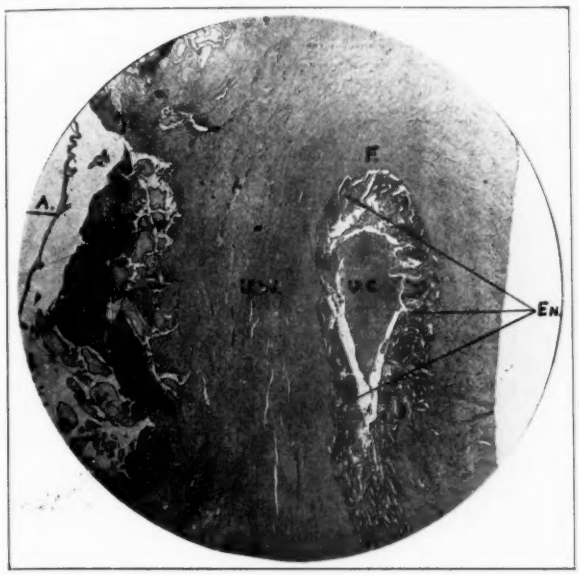

Fig. 31.—Section through the interstitial pregnancy on the right, showing the amniotic cavity at (*A.*), with its surrounding chorionic villi (*C.V.*), imbedded in the uterine wall (*U.W.*). The uterine cavity (*U.C.*) is to the left, lined with a thickened endometrium, (*En.*) which extends from the fundus (*F*) down to the internal os.

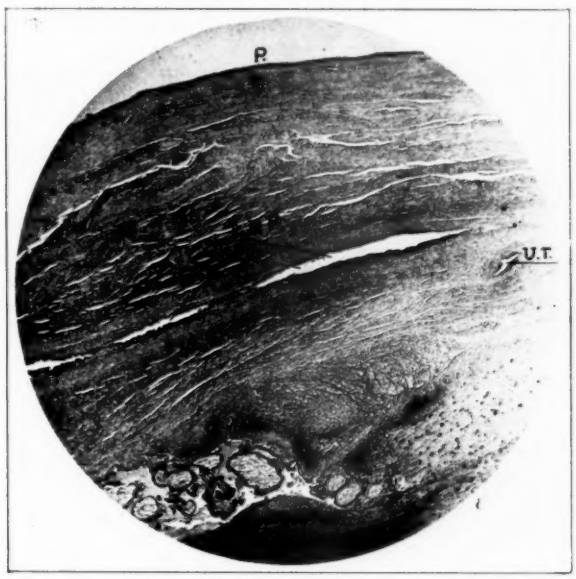

Fig. 32.—Section of the interstitial pregnancy showing the gestation site (*G.S.*) below, deeply imbedded in the uterine wall; the interstitial part of the fallopian tube (*I.P.F.*) running longitudinally in an inward and upward direction, to its uterine termination (*U.T.*), which is characterized by the triangular outline of its lumen, and by the circular arrangement of the muscle fibers around it. The peritoneal covering (*P*) is normal.

pronounced decidual reaction, which was also accentuated in the walls of some veins (Fig. 29), directly under the endothelial lining. Some blood vessels were filled almost to capacity with trophoblastic material (Fig. 30). The uterine cavity (Fig. 31) was lined with an endometrium characteristic of intrauterine pregnancy, it only lacked the trophoblastic constituents. The interstitial gestation bears no anatomic relation to the uterine cavity or to the tube lumen, as seen in Fig. 32, the latter lay above and to the inner side of the ovular bed. The very terminal portion of the fallopian tube was indicated by the triangular outline of the lumen, which was surrounded by a number of concentrically arranged muscle fibers. No evidences of a chronic salpingitis were found. Epicrisis: The absence of any anatomic relationship between the uterine cavity and the ectopic bed proved conclusively its true interstitial character. Further supportive evidence was the anatomic relation which the round ligament bore to the seat of the pregnancy. The reason the gestation area appeared completely outside the tube lumen, giving the impression that the tube was never its seat, was most probably due to the thinness and narrowness of the wall of

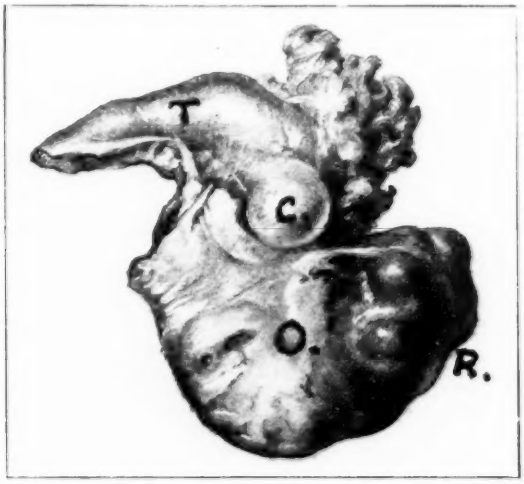

Fig. 33.—Primary ovarian pregnancy. The fallopian tube (*T*) is normal, excepting for the small mesenteric cyst (*C*) near its fimbriated end. The ovary (*O*) is enlarged, its outer half is suffused with blood, and at point (*R*) the rupture took place.

the interstitial part, through which the burrowing ovum passed readily and lost its anatomic connection with it. The absence of uterine bleeding and the nausea which persisted up to the time of operation and the very moderate intervillous bleeding, indicated that the ovum was still alive, at that time. The pain in this case was due mainly to the uterine twist caused by the pedunculated subserous fibroid.

CASE 9.—*Primary Ovarian Pregnancy, Ruptured.* R. K., age twenty-seven, married six and a half years, has had one premature birth at six and a half months, five years ago; one full-term terminated by cesarean section four years ago; and one induced abortion two years ago. Menses began at fourteen years, twenty-eight-day type, lasting five days, profuse and painful, the last period occurred on Sept. 18, 1922. On Oct. 9, considering herself gravid she had an abortion induced. The attempted interruption of her pregnancy was followed by uterine bleeding on the fourth day thereafter, the amount was moderate, and it lasted for several days. On Dec. 4, while at stool she was seized with a sharp pain in the pelvis and became un-

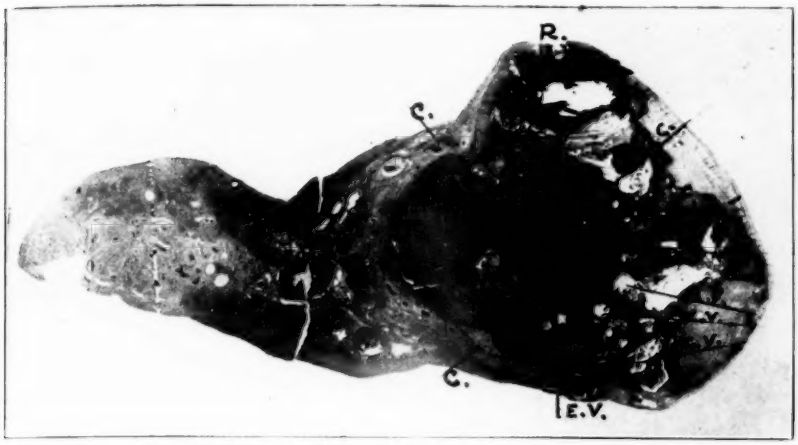

Fig. 34.—Longitudinal section of the ovary harboring the pregnancy. The gestation mass occupies the outer enlarged half, it consists of blood clot (*B.C.*), chorionic villi (*C.V.*), and the remains of the embryonic vesicle (*E.V.*) about the center of the mass. The capsularis (*C*) is formed by the ovarian stroma. (*R.*) indicates the site of rupture.

Fig. 35.—High power reproduction of the rupture point in the primary ovarian pregnancy. The rupture is at *R.* and the pregnancy, indicated by the mass of chorionic villi (*C.V.*) many of which have undergone hyaline changes, is located in the depths of the ovary. The capsularis (*C*) is made up of the following constituents, tunica albuginea (*T.A.*), ovarian stroma (*O.S.*), fibrin (*F.*), and blood clot (*B.C.*).

conscious. I saw her within an hour after the onset of the above symptoms. Inspection showed an exsanguinated patient, with a small fleeting pulse, cold clammy skin bathed in perspiration, and a clouded sensorium. The diagnosis of intraabdominal bleeding was so evident that no time was wasted in making a vaginal examination. After administering a dose of morphine hypodermically she was dispatched

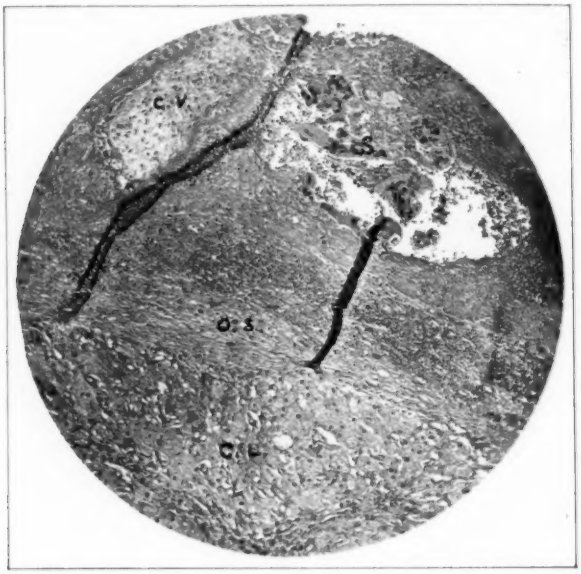

Fig. 36.—Primary ovarian pregnancy. The corpus luteum (*C.L.*) is separated from the gestation mass, consisting of clumps of syncytium (*S.*) and chorionic villi (*C.V.*), by a broad strip of ovarian stroma (*O.S.*).

Fig. 37.—Blood vessel (*B.V.*) wall in ovarian pregnancy showing a subendothelial decidual reaction (*D.R.*).

with all haste to the hospital and directly to the operating room. As soon as the operative field was prepared I performed a laparotomy and found the abdominal cavity filled with blood, which came welling up from a rupture point in the outer pole of the left ovary. The left adnexa were removed, the uterine end of the right

tube resected, to prevent further conceptions, the free and clotted blood evacuated, and the abdominal incision closed. The recovery was uneventful. The specimen (Fig. 33) consisted of the left uterine adnexa: the fallopian tube was normal, its abdominal end patent and free, and the mesosalpinx the seat of a small mesenteric cyst. The ovary measured 4 by 2.5 by 1.5 cm. Its outer half was dark blue in color, due to suffusion of blood into the stroma, the hemorrhagic portion measured 1.75 by 2 by 2 cm., nodular, the tunica albuginea tense and in its upper and outer quadrant was the point of rupture, as large as a split pea. The outer two-thirds of the ovary (Fig. 34) harbored the ectopic pregnancy, consisting of blood clot, chorionic villi, trophoblast and débris. The capsularis (Fig. 35) was formed by the ovarian stroma covered externally, except at the point of rupture, with the germinal layer, and on its inner surface was in contact with the products of gestation. The corpus luteum of pregnancy (Fig. 36) did not form a direct constituent of the capsularis, but lay to one side of the gestation area. A subendothelial decidual reaction was present in the walls of some of the blood vessels (Fig. 37), whose lumina were

Fig. 38.—Primary abdominal pregnancy, located in the cul-de-sac of Douglas. The uterus and its adnexa are normal.

free from trophoblastic elements, while those containing chorionic villi did not show this proliferation. Epicrisis: The normal condition of the tube, the absence of any adhesion between the fallopian tube and the ovary, and the location of the pregnancy within the ovarian stroma, constitute the cardinal morphologic facts, determining a true ovarian pregnancy. It is also very instructive to bear in mind the topical relation of the corpus luteum to the capsularis, about which more will be said later.

Case 10.—*Primary Abdominal Pregnancy with Intracapsular Rupture.* M. D., age twenty-six, married five years, had one child four years ago and one spontaneous abortion in the fourth month of pregnancy, three and a half years ago. Menses began at the age of thirteen, twenty-eight-day type, lasting two days, painless and scanty; the last period occurred on April 28, 1925. For the past six months she suffered from a progressively increasing dysmenorrhea and oligomenorrhea. Her relative sterility is voluntary. On May 12, she was taken ill with sharp pain in the

lower pelvis radiating to the rectum; this attack lasted for several hours. On May 30, she had another attack and the following day began to stain and expel clots, this bleeding lasted two days. Since June 1, she complained of a constant pain in the

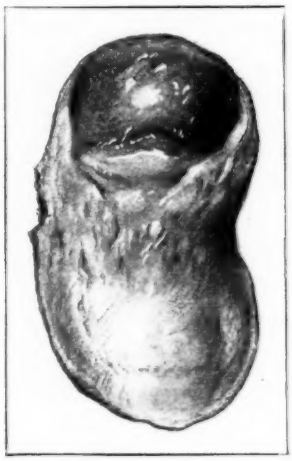

Fig. 39.—Primary abdominal pregnancy. Its surface is smooth, covered by serosa, excepting at the points where it was attached to the adjacent viscera.

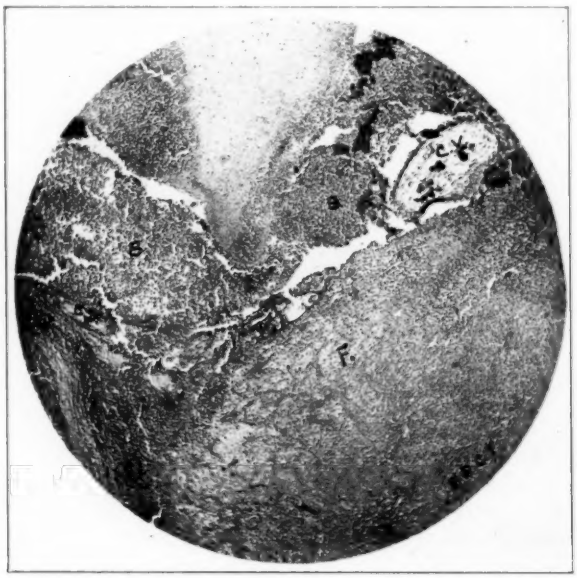

Fig. 40.—Primary abdominal pregnancy, showing the chorionic villi (*C.V.*), the free blood (*B*), the fibrin (*F*), and other products of gestation surrounded by the edematous and infiltrated subperitoneal connective tissue (*S.P.C.T.*) layer

lower abdomen, which was worse on walking and during defecation. Physical examination June 9, revealed tenderness over the lower half of the abdomen, no peritoneal rebound, a sausage shaped tender mass in the posterior culdesac, with the uterus displaced upwards and to the left. A diagnosis of left tubal pregnancy was made

and a laparotomy performed the same day. Operative findings: The uterus and its adnexa were normal to inspection and palpation, no blood escaping from either the tubes or the ovaries, and the pelvic contents were very slightly tinged with blood. In the rectouterine space (Fig. 38), an oblong dark bluish tumor mass was present, partly attached to the lower uterine segment anteriorly and to the wall of the rectum posteriorly. Its separation from these fixed points was followed by a moderate amount of oozing which was readily stopped by compression. The specimen (Fig. 39) was bluish red in color, resembling in outline a miniature kidney, it measured 3.5 by 1.5 by 1.25 cm., its surface was smooth excepting at the point where it was attached to the adjacent organs. The cut surface presented the familiar appearance of a blood clot, enveloped by a thin membrane. Within the meshes of the blood clot (Fig. 40) many chorionic villi were seen, in different stages of degeneration, surrounded by a capsule made up of the peritoneal and the subperitoneal connective tissue coats. The outer surface of the capsularis was covered with low cuboidal epithelium, the subperitoneum infiltrated with round cells and blood cells, and the inner surface in contact with the gestation elements.

Epicrisis: The nonparticipation of the uterine adnexa in the formation of the gestation mass, and the subperitoneal nidation of the ovum, established the diagnosis of a primary abdominal pregnancy, beyond the shadow of a doubt.

(To be continued.)

(For discussion see page 143.)

THE DIFFERENTIATION OF CANCER TISSUE*

By James E. Davis, A.M., M.D., Detroit, Mich.

THE subject will be discussed under three subtopics: (1) The antagonistic and synergistic factors in cancer; (2) The characteristics of cancer tissue; (3) The specific morphologic unit changes in malignancy.

ANTAGONISTIC AND SYNERGISTIC FACTORS IN CANCER

That the body possesses means for protecting itself against cancer is evidenced by the fact that no natural cause of this disease is 100 per cent effective. The two correlated questions are frequently asked: Why does not everyone have cancer, and why do some persons have cancer? It is obvious from statistical studies that a clergyman or a farmer have much less chance of dying from cancer than have industrial laborers. It is also obvious that there is a closer causative relation of this disease to certain occupational irritants and not to others, for workers in paraffin, dyes, etc., are frequently affected, while those working with lead never or very rarely have cancer.

While statistics easily prove that cancer is most common between the ages of fifty-five and sixty years, yet it grows best in young healthy animals and in their well vascularized tissues.

It would seem as if resistance here should be maximal. On the

*Presented at the Thirty-eighth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 16, 1925.

Fig. 1. Right.

Fig. 1. Left.

Fig. 1.—Scirrhous carcinoma of the mammary gland. *Right.* This new growth has stimulated the production of an unusual amount of stroma. The epithelial cells are massed in irregular forms. The individual cells differ in size and form. The nuclei vary in absorption of the stain and preservation.

Left. The same tumor as shown on the right actively differentiating in axillary lymph node tissue. The same type of tumor cell can be easily recognized, but the modifying influence of a tissue with but little stroma is quite evident.

contrary, results have shown that even if tissue resistance per se is high, growth impulse of the malignant tissues is higher, owing to superior nutrition supplied their abnormal cells functioning only for growth and multiplication. In old age, lowered function, diminished nutrition, and general biologic conservation are not antagonistic to the causes of cancer, but they are factors impeding its growth.

Much has been said concerning the influence of certain articles of diet aiding the differentiation of cancer tissue, yet no satisfactory proof of this is supplied by vegetarians or by excessive meat eating peoples of Argentina, Australia, and New Zealand, or the meat consuming Eskimos. Horses and cows are exclusively vegetarian animals, but they frequently have cancer.

The effort to attribute the causative background of cancer to heredity and to effects of civilization has not succeeded. In very recent literature many attempts have been made to show that primitive peoples are remarkably free from this disease. The evidence gathered has lacked data very essential for satisfactory proof of this contention. The primitive people applying for medical examinations are relatively few in number and the number reaching and passing the average cancer age is small. The number of necropsies performed upon primitive people is necessarily small. Hoffman[1] has directed attention to the interesting fact that Scandinavia and Switzerland obtain 90 to 100 per cent autopsies, and it is in these countries the cancer death rate is highest.

It must be admitted that blood and tissue resistance to cancer is only relative, for even splenic, muscle, nervous and lymphatic tissues grow cancer, and so also do the tissues in cases of lymphatic leucemia. The fact that a positive and absolute autogenic control of cancer is possible needs no other proof than is afforded when the fetus in utero dies and the somatic control substance causes cessation of chorionic growth even in malignant chorionepithelioma.

The experimentalist, working intensively in a favorable field, can break down the resistance of nearly every mouse to cancer by a sufficient number of applications of tar, but men and mice both need to have their skin irritated for about one-fourth of their lives before there is much liability of its becoming cancerous.

Ewing[2] sums up the restraints to growth, saying they have at least four factors:

1. Mechanical pressure of cells on each other
2. The distribution of nutriment
3. The influence of specialized functions
4. Organization

In discussion of these factors he aptly comments upon No. 2, saying: "There is extreme fibrosis of the ovaries in many cases of mammary

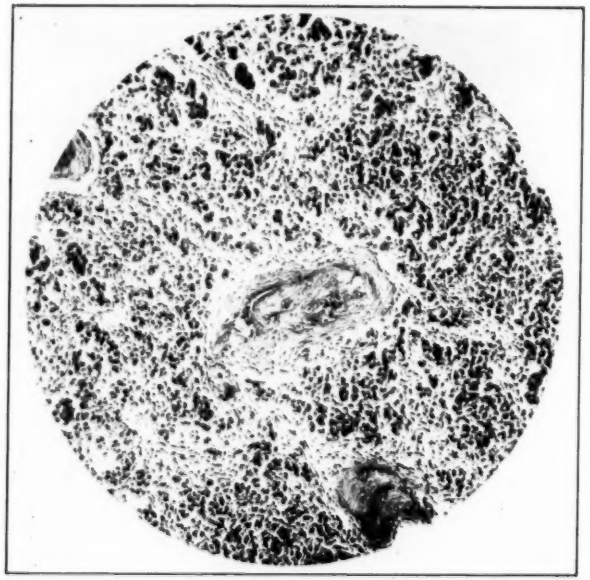

Fig. 2. Left.

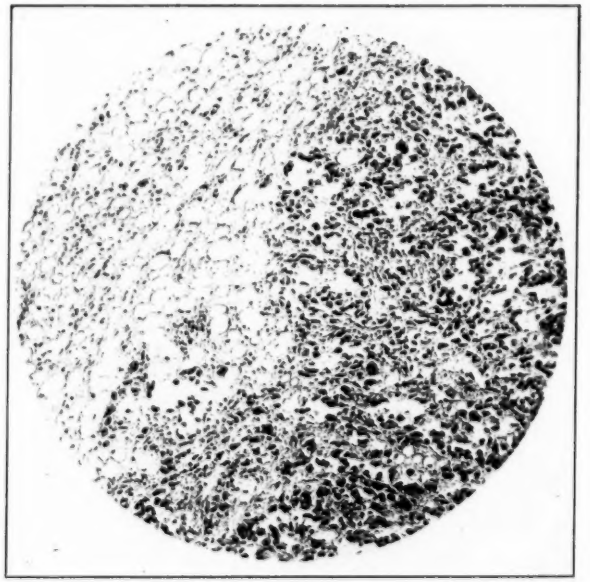

Fig. 2. Right.

Fig. 2.—Carcinoma in liver and fat tissue.

Right. Approximately the right one-half of the section is infiltrated with poorly differentiated tumor cells and but slightly formed tubular glands. In this loose areolar fat tissue the antagonism to differentiation is less than in the companion picture on the left, where the growth is in liver structure.

Left. The perilobular vascular structures are not yet invaded, mainly because of their muscle tissue.

cancer," and upon No. 3 as follows: "Normal function diverting the energies of the cells must be a constant restraint or regulator of growth. In most organs certain groups of cells are set apart for growth, e.g., germ center cells of lymph-nodes, cells at bases of intestinal villi, and the basal cells of the epidermis." He illustrates *Organization* (No. 4) by pointing out that "all known features of a malignant neoplasm are exhibited by the normal chorion, even the destructive invasion and cachexia, but the process is not a tumor *because of its purpose* which shows it is under control of the organization."

CHARACTERISTICS OF CANCER TISSUES

The cancer of one individual differs from the cancer of another individual just as widely as do their respective tissues, and so does the malignant growth in one organ differ from that in another organ. Also, the new growth arising in one tissue will usually strive to repeat the morphologic type of its mother tissue, but, as it differentiates new cells in another though contiguous structure, the conformation to its new environment may be unusually close. The rapidity of a malignant growth in different tissues may vary with the richness of blood supply, the irritation it sustains and the tissue in which it grows. Cancer will grow in muscle and splenic tissues, but it is seldom found thriving in such structures. It is interesting to remember in this connection that the liver, the largest gland of the body, is infrequently the site of primary cancer growths. This is especially true throughout America and Europe, but in the Orient there is relatively considerable frequency of its occurrence even in children.[3] The general infrequency of liver cancer may be due to the liver's increased ability to fix and render foreign proteins harmless.[4]

Then again, malignant tumors may grow well in fat tissue but do not easily originate there.[5] It is claimed that the groin and the upper part of the thigh are the most common seats of atypical lipomatous tumors (liposarcomas).

There is a marked variation in the frequency of cancer in the different tissues. Wilson[6] has compiled 1,430 cases of malignant tumors of the thyroid from the world's literature prior to 1921. In 74,335 necropsies the frequency of malignancy of the thyroid was 1 in about 385, and the majority of these tumors seemed to be primary. A metastatic involvement of the thyroid is considered a curiosity, and metastasis of hypernephroma to the thyroid is the rarest of all tumors so metastasizing.[7] Metastasis from the thyroid takes place early and quickly into bone and other tissues.

Carcinomata of the head and face tend to remain local, but it is estimated that 90 per cent of skin cancers develop on the unprotected

Fig. 3. Left.

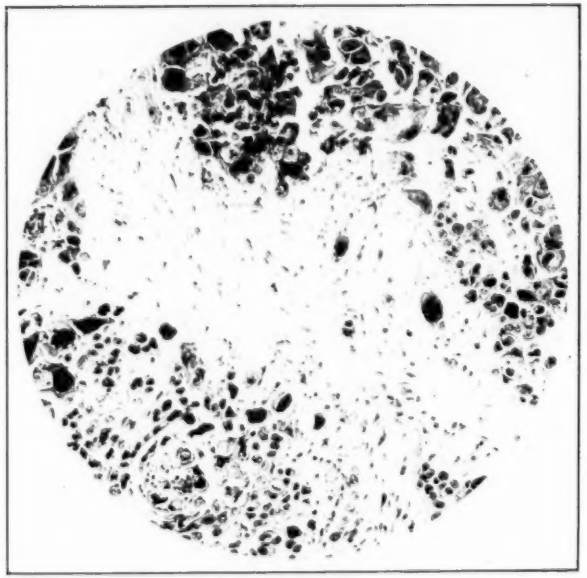

Fig. 3. Right.

Fig. 3.—A polymorphous epidermal carcinoma of the esophagus. The growth involved both the mucosa and muscularis causing a board-like rigidity of the tube from the lower border of the thyroid to the level of the tracheal bifurcation.

Left. The stratified epithelium extends deeply by tongue-like processes into the submucosa. The regularity of the basal cell layer has changed. A sharp contrast is seen between the organization prevailing in the greater portion of the left and right halves of the field. Variation in size and shape of the cells is apparent.

Right. In this field the unusual number of large cells and a central band of newly grown connective tissue are seen.

parts of the face and neck. The lower lip is said to be the site of 33⅓ per cent of all skin cancers.

Bell[8] says: "Malignant neoplasia in the human is a biologic atavism."

Rohdenburg[9] states: "The basic difference between a malignant and benign cell is continuity of cell division without cessation. Cells are killed when the chronic irritant acts upon the tissue. A neoplasm starts after chronic irritation in a susceptible tissue. Emphasis is placed upon the susceptible tissue or susceptible individual, for this seems to be the all-important factor. The killing of cells is repeated and repeated within the same small area. When the tissue cells die, they either become acid or less alkaline than the adjacent living cells. As the dead cells autolize, the product becomes more acid. The body fluids tend to neutralize this acidity and ultimately a growing tumor demineralizes the body. This added inflow to the cell creates a chronically overfed cell with resulting division and repeated division.

"Dead homologous protein, with the living and dead heterologous protein, hypermineralize the blood and the cancer cell contains 10 to 13 per cent more salt than does the normal cell. Neoplasia, then, is a condition of changed metabolism, characterized by hypermineralization."

The essential factor in the precancerous change is the condition of the connective tissue. Epithelium cannot nourish itself properly from the body fluids without depending upon the connective tissue for nutrition: it might be described as an obligate parasite on connective tissue. It cannot grow by itself without the addition of the connective tissue. In this connection, Wood[10] has observed that the stroma, which is a nonspecific comparatively inert connective tissue, supports the blood vessels, and this is the only functional relation of the normal and the tumor tissues, lymph vessels and nerve fibers being usually absent. The quantity of stroma appears to depend upon the stimulation given by the parenchyma, and tumor tissue parenchyma grows more rapidly than its stroma. Bashford[11] believes: "The cancer cell is a biologic modification of the normal cell endowed with many inherent properties of the latter. But it has ceased to be functionally important to the body. In form it varies from the normal but slightly and then on to the unrecognizable. In organization, the definite plan followed by all normal cells is abandoned and the body is depended upon only to supply the tumor cells with nutrition."

W. Blair Bell[12] observes that: "Whatever causal factor, whether metabolic or extrinsic, can permanently impair the cell without killing it, may be regarded as a predisposing cause of malignancy." And further: "What happens to and in a cell driving it to adopt an unnatural, malignant course of life? A healthy cell does not do this, a dead cell cannot. There is, however, an intermediate state."

Greenough[13] summarizes the factors that enter into the determination of the degree of malignancy of cancer of the breast as follows:

1. By histologic study of the original tumor, three classes, low, medium and high malignancy can be distinguished.

2. Degree of differentiation.

3. Degree of secretory activity, as shown by vacuoles and droplets of mucoid material.

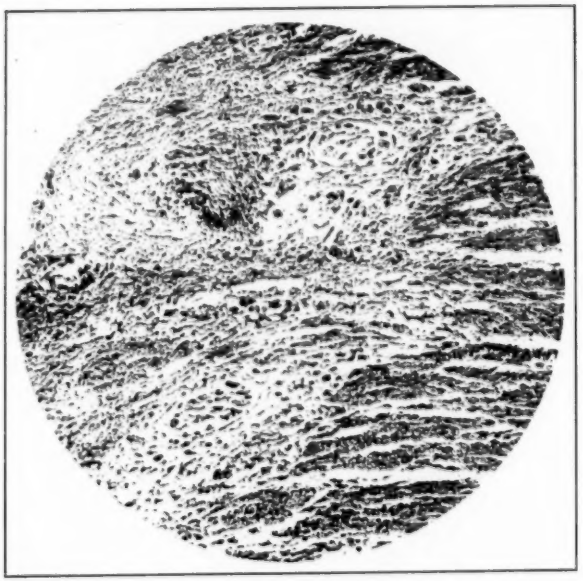

Fig. 4. Left.

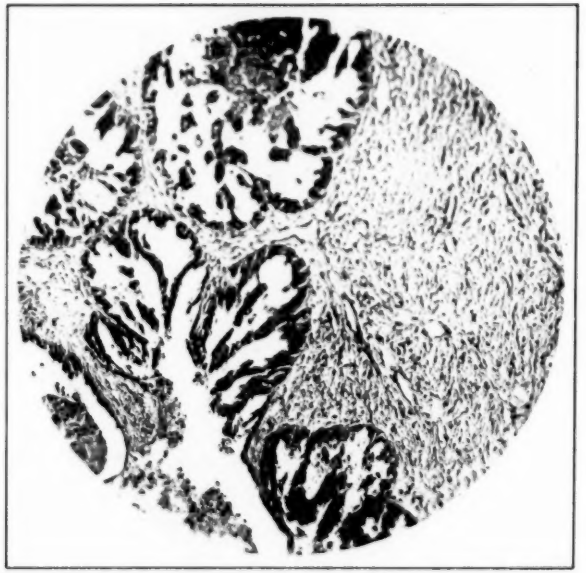

Fig. 4. Right.

Fig. 4.—Adenocarcinoma of the sigmoid colon.

Left. Undifferentiated new-growth cells invading the muscle tissue.

Right. The new growth is differentiated into abnormally shaped glands, and the individual cell units are irregular and incompletely arranged. The marked tendency to degenerate is quite evident. The compactness of the stroma and aged appearance of the cell nuclei can be plainly seen.

4. Uniformity of size of cells and of nuclei, as opposed to variation in size.

5. Absence or presence of hyperchromatic changes in nucleus and few or many mitotic figures and whether irregular or not.

6. High malignancy is shown by cells and nuclei of irregular shape and size without secretory function, and arranged in solid columns, large or small together, with numerous and irregular mitoses and hyperchromatism.

7. Round-cell infiltration indicates cell degeneration rather than resistance.

8. Hyalinization of the stroma is a factor of age rather than of resistance.

Though there is infinite variety in the forms of cancer, yet there are certain features based upon principles of construction common to all, viz.:

1. It begins at one point.

2. It begins as a local disease.

3. It spreads centrifugally by permeation and embolism.

4. All cancers are composed of cells with type characteristics imitating the tissue in which they began.

5. All cancers are distinguished by a reversal of development shown in the inferiority of their cells, which appear unfinished and even embryonic. The more simplified or debased, the greater the malignancy.

6. The shape, size, internal construction and staining properties of the cancer cell and nucleus approach those of the cell and nucleus of embryonic, vegetative or unicellular type.

7. The highest degree of malignancy as a rule goes with the most cellular neoplasms, and the smallest and roundest cells, which stain intensely and show very active mitoses resembling some vegetable cells.

8. The reduced cells of the cancer are more akin to the lower class cells than to the cells of the higher order from which they sprang, and are therefore not so chemotropic to them.

9. Normal embryonic tissues cultivated in vitro continue to grow indefinitely, whereas in similar circumstances cancer cells undergo molecular degeneration.

10. Cancer cell degeneration is correspondingly as rapid as its generation.

11. Molecular decay is conspicuous in cancers injured or exposed to bacterial invasion.

12. Cancers outrun their blood supply.

13. Cancer cell proliferation is always a backward and never a forward change.

14. Cancer excites local tissue opposition.

The most important structural characteristics of cancer are those which show reversal and incompleteness of type. The cells do not become embryonic but they do become embryonoid. The degeneration change is but partly completed. It stops short of molecular degeneration in its regressive movement and proceeds to multiply incessantly. It is the only form of senilism which (1) begins locally in independent cells and (2) spreads centrifugally with but little regard for anatomic boundaries.

The dissemination of tumor cells into the vascular coats, according to Goldmann,[14] is effected by blood vessels. "In arteries the tumor cells rarely proceed further than the outer coat, whereas in veins they are generally found beneath the intima." Tumor-cell infiltration then

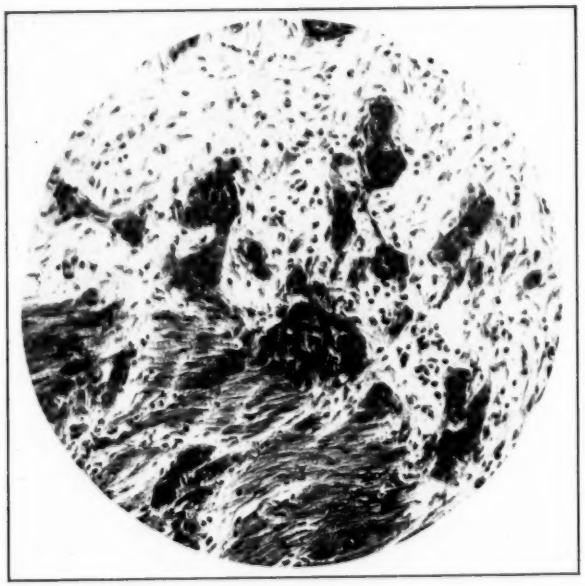

Fig. 5. Left.

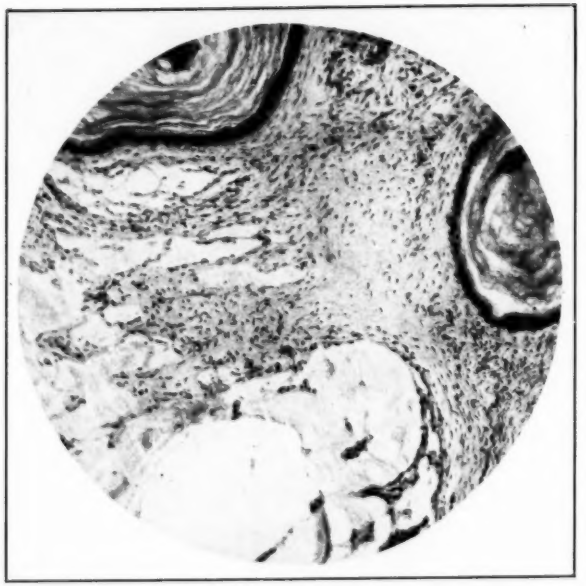

Fig. 5. Right.

Fig. 5.—Carcinoma of the mammary gland and pectoralis muscle.

Left. The lower left one-third of the field shows the muscle with consuming cancer cells in mass formation. The remaining two-thirds of the tissue shown has been transformed into connective tissue structure excepting where masses of cancer cells prevail.

Right. Interductal aged stromal tissue with dilated ducts. On the left side the ductal epithelium is markedly degenerated and mucoid degeneration prevails.

into the walls of channels bounded by elastic tissue is a feature characteristic of malignant tumors only.

It is accepted that the vasa vasorum in arteries remain within the limit of the outer coat, rarely branching into the superficial layer of the middle one, whereas in veins they extend beyond the middle coat into the region of the intima. In fetuses and newborn infants there is no material difference between arteries and veins as regards their nutrient vessels, but after the first year the differentiation is accomplished. Virchow observed that arteries act as isolators of pathologic processes, but all this is changed as soon as pathologic processes arise in the artery from within or without. Then the connective tissue, and above all the vasa vasorum, begins to proliferate.

The second important point is that the regular distribution of blood vessels is disturbed by the invading growth. Tumors may show an extensive new formation of blood vessels. This is most important in the zone of proliferation, which in infiltrating tumors is at the periphery.

An infiltrative growth causes great commotion in surrounding blood vessels, particularly in strongly vascularized tissues, such as mammary gland or muscle. The vessels are dilated, thrown into spirals, and develop numerous capillary offshoots towards the invading growth. In cancer the vessels are arranged almost entirely in the peripheral area. As the volume of growth increases, the vessels decrease. In necrosis the vessels tend to disappear totally.

In sarcoma, the numerous vessels are evenly distributed throughout the entire growth as a delicate, closely-woven network.

Bashford demonstrated that the stroma of experimental tumors owed its origin to the inoculated animal, but the structural characteristics of the stroma are determined by the tumor cells.

When the vascular reaction is below normal or fails to take place, Thiersch has called this premature senescence of the connective tissue in cancer.

Reactive power is judged by the stroma formation as well as by degeneration.

SPECIFIC MORPHOLOGIC UNIT CHANGES

Differentiation is change from the general to the special—in type of cell, type of tissue, type of organ, and type of animal. During the developmental and so-called fixed states, antagonism exists between epithelial and connective tissues. Broders, Judd[15] and others have used the degree of differentiation to estimate the grade of malignancy, e.g., if there is 75 per cent differentiation and 25 per cent without differentiation, the cancer belongs to Grade I (mildest type). If differentiated and undifferentiated tissues are equal, the malignancy belongs to Grade II. If 75 per cent of the tissue remains undifferen-

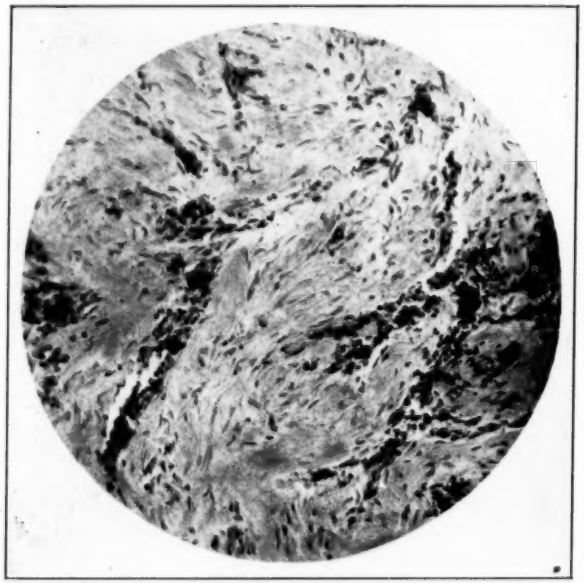

Fig. 6. Left

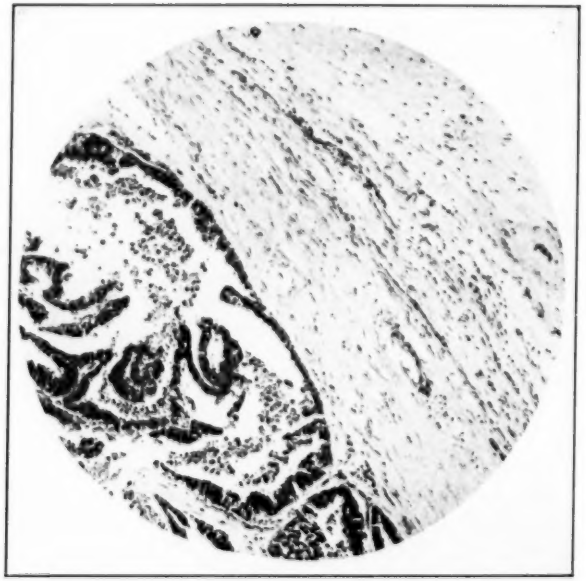

Fig. 6. Right.

Fig. 6.—A papilliferous cyst adenocarcinoma of the ovary.

Left. An area of firm stroma with irregular masses of invading carcinoma cells without differentiation, comparable to that seen on the right section.

Right. Compact, aged stroma on the left with bizarre gland forms on the right rapidly degenerating.

tiated, the cancer is called Grade III. When there is no differentiation, then malignancy is severest.

Besides the degree of differentiation, the type of cell can sometimes indicate the degree of malignancy. Martzhoff in 1923 studied the histomorphology of predominating cells in epidermoid cancer of the cervix uteri and concluded that the spindle-cell type was least malignant, the transitional cell more malignant, and the fat spindle-cell type most malignant of all. Epithelial tumors depart less from the primordial type, hence their cells still retain their primitive powers of growth and multiplication in a higher degree than others.

MacCarty[16] believes the body is composed of at least forty-five different types of cells, characterized by evolution, fertilization, segmentation, differentiation and specialization.

Differentiation is divided into three recognizable stages:

1. General alignment of cells (as in the normal adult tissue in undifferentiated form).

2. Cellular polarity (as in fully differentiated tissue).

3. Adult morphology.

In postoperative cases of cancer MacCarty observed life was prolonged when differentiation was present. This was especially true of skin cancers, for the cases without differentiation lived 274.7 days, while those with differentiated tissue lived 534.1 days, or 259.4 days longer.

Levine[17] states that "uninucleate or multinucleate giant cells constitute an important part of cancer tissues. That these cells may give rise to pluripolar spindles and hyperchromatic cells is likely. These cells are not degenerating cells, as claimed by earlier workers, but are found associated with some increased metabolic process in the growth of the malignant neoplasm. Malignant neoplasms in man are characterized by rapidly dividing cells with aberrant types of division. The cells that make up the growth may have developed in situ or have come through the blood and lymph channels from distant parts of the body. These cells are endowed with a progressive proliferating power and die with the host. Plant overgrowths resulting from infection with B. tumefaciens, etc., are due to rapid but normal division of cells. Atypical divisions are not found in these tissues. All cells in infectious plant neoplasms differentiate, reach maturity, become senile, and die independently of the host."

Fischer[18] of Copenhagen has shown that in the culture of fibroblasts the average of mitotic cell divisions in a given time in the peripheral zone was 2 per cent, and Haberlandt[12] found in the cultivation of plant tissue cells in vitro that single isolated plant cells were not able to divide until they were in contact with certain other plant tissue elements, but various types of sarcoma cell are able to divide in vitro when isolated and scattered.

While malignant cells have been cultivated in vitro by Carrel and Burrows[20] (chicken sarcoma, rat sarcoma and the Flexner-Jobling rat carcinoma) Lambert and Hanes[21] (mouse carcinoma) and Losee and Ebeling[22] (a human sarcoma), all agree that it is rather difficult to keep tumor cells growing outside the body. Living cells require minute quantities of certain special substances derived from organic matter to maintain life and active proliferation. Therefore the rate of growth of tumors in animals can be appreciably increased by inoculating a substance derived from the breaking-down products of tumor cells. It has been known for more than fifteen years that two apparently opposite biologic effects may result from the absorption

of tumor material. An animal may become effectively protected against tumor growth, or it may become sensitized so that a tumor grows in it more rapidly than in a normal animal.

Sokoloff[23] distinguishes two kinds of cells in cancer tissue. One type is related by its qualities to the cells of the embryo. Such cells are active, possess a high degree of vitality, and probably cytologically and morphologically are closely related to embryonal cells. The second type of cells observed in tumors are those which exhibit a condition of disintegration of the formed elements so that the normal morphology is entirely distorted by these probably dying cells. The character of the tumor, its size, and the degree of its malignancy, are in a considerable measure determined by the correlation between the cells of these two types.

A large number of writers, including Sokoloff and Cartotto[23] have observed the glycogenesis of cancer cells and the importance of the cellular lipoids in relation to cellular anarchy and cellular activity. Studies of the mitochondria in tumors show

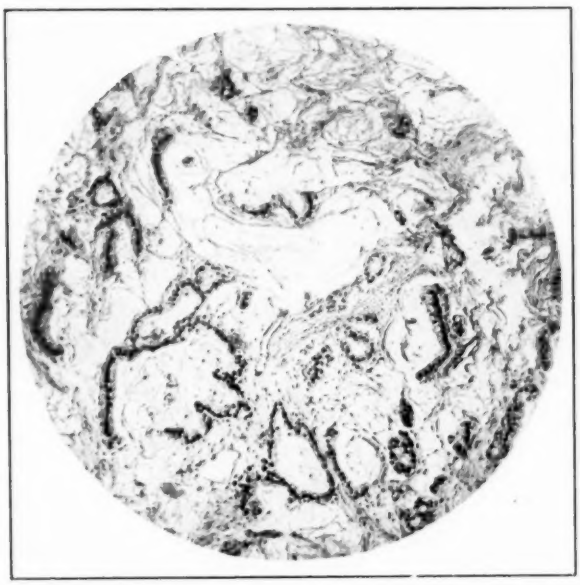

Fig. 7.—Carcinoma gelatinosum. This tumor was characterized by rapid growth, large size and a corresponding rapidity of degeneration. The production of mucus exceeds the amount of stroma and epithelium in the field. The epithelial cells and their organization into gland forms show good differentiation.

that their biologic and physiologic properties are correlated with those of healthy cells in a state of active growth. Cancer cells can be divided into four types:

1. Young cells with small nucleimitochondria, absent or almost invisible.
2. Strongly marked embryonic characters and larger nucleimitochondria, larger in number and size, appearing as rods or granules.
3. Depressed cells with indistinct nuclear outlines, mitochondria almost invisible.
4. Cells in the course of complete disintegration.

Ewing[24] says: "Embryonal cells possess more than any others the essential factors of tumor growth. This is perhaps the most important single fact of our knowl-

edge of tumor genesis. It would seem that tumor genesis were chiefly a question of the mechanics of development. The complete emancipation of malignant neoplasms from the normal laws of growth *remains the obscure and essential element.*''

Ribbert[25] has insisted that no unusual power of proliferation exists in cancer cells, that these cells freed from the restraints of tissue tension are merely exhibiting the powers of growth with which they are endowed from the ovum.

SUMMARY

1. Cancer cells or cancer tissue cannot be differentiated either in vivo or in vitro from dead cells or from normal cells.

2. Two genetic sources undoubtedly supply the units of cancer formation, namely the injured and the embryonic cells.

3. It is plausible to believe that heredity may supply in certain families and individuals protoplasm of low potential quality for ultimate differentiation, and the physical evidence will appear in the abnormal number of cells unable to gain maturity.

4. The preponderance of evidence and modern opinion point to irritation, regardless of its type (whether traumatic, thermic, chemical, bacteremic or parasitic), as the exciting cause, which can act with equal facility upon embryoid or atavistic type of cells in producing uncontrolled, incompletely organized, dysfunctioning tissue.

5. Under the conditions prevailing in cancer, function no longer determines form, but conversely, form determines function, which is inadequate, abnormal and superfluous.

6. With inadequate tissue organization, lacking as it does nerve and lymph supply, and possessing a precarious blood vessel canalization, supported by an uncertain stroma and exercising free parasitic characteristics, there can be little wonder that degenerative changes are constant.

7. The chemical activities of cancer tissues tend towards acidification of body fluids with consequent body demineralization and cancer tissue hypermineralization.

8. The differentiation of cancer cells can be advantageously studied by estimating both the number of the new growth cells differentiated and their nearness or remoteness to normal standards of form.

9. Observation of the cell division figures and the degenerative changes in nuclei affords useful information as to rapidity of growth.

10. It should be expected that cancer cells will differentiate after the pattern of their parent tissue, but frequently the influence of a new environment compels a close resemblance to surrounding structures but occasionally no imitation of either is recognizable.

11. The kind of food consumed or the mode of life pursued have but little to do with the development of cancer.

12. The better nutrition supplied by younger subjects is the greatest factor in producing a maximal growth impulse in malignancy.

13. Growth, pressure, nutrition, specialized function and organization, all represent central, general, purposeful provisions for the body, but malignant growth has no purpose in the body economy.

14. The cancer tissue may repeat or depart from its pattern form. It may or may not be influenced by its environmental structures.

15. Tissue susceptibility to cancer varies widely and metastasis from different anatomic locations is often distinctive.

16. The connective tissue is the only functional relation of the normal to the tumor tissues and reaction to the cancer can be judged by the stroma formation as well as by degeneration.

17. As epithelial cells depart less from their primordial type, they consequently have a greater potential and actual growth impulse.

18. *Differentiation, which is a change from the general to the special in type of cell, tissue, organ, and animal, is always incomplete in all four types if it is cancer tissue.*

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111 JOSEPHINE AVENUE.

(*For discussion see page* 122.)

THE CLINICAL AND PATHOLOGIC FEATURES OF PUBERTY HEMORRHAGE

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PUBERTY bleeding clinically designates menorrhagia or metrorrhagia occurring early in menstrual life. These abnormalities are locally independent of inflammation, neoplasia and the pregnant state, as well as of the varied blood dyscrasias. They are closely allied to the essential bleeding occurring at the menopause and clinically as well as pathologically both forms overlap. In this communication the puberty group is stressed.

A review of 26 cases from the gynecologic services of the General Memorial and Long Island College Hospitals emphasizes the following characters of this disease.

1. Primary menstrual anomalies: Both menorrhagia or metrorrhagia may set in as the initial epoch of sex life or supervene more slowly following oligomenorrhea, hypomenorrhea or other disorders of menstruation.

2. Absence of abnormalities in the general physical examination: This is true in the great majority of cases; yet two in this series showed definite endocrine dyscrasia. Though only fourteen years of age, both of these girls were fully matured, with mammae well formed, the external genitalia fully developed, and the uterus large. The unusual height, 5 ft. 10 in. in one and 5 ft. 6 in. in the other were indicative of abnormal pituitary stimulation.

3. Normal bleeding and clotting time. These tests were performed where secondary anemia was unduly severe and as a rule prior to transfusion. In six instances the findings were within the normal.

4. Pelvic abnormalities: In all cases, the cervix was found unusually soft and patulous. In addition several were noted with enlarged uteri. In all the curettings were abundant and hyperplastic.

5. Recurrence of symptoms after curettage was the rule where abrasion was performed as a therapeutic measure.

6. Excellent therapeutic response, with control of symptoms by radium was universal, even though small quantities were employed.

These features are well demonstrated in seven typical cases abstracted below.

Case 1 (L. I. C. H., 1921, No. 2966).—Menorrhagia the initial epoch of menstrual life, persisting until relieved by treatment.

Miss M. H., aged fourteen years, was admitted to Dr. Gibson's service at the Long Island College Hospital, June 9, 1921. Her first menstruation began profusely one month before and continued to date of admission. Hemoglobin, 30 per cent; bleeding and clotting time normal. Physical examination was negative. Under anesthesia the pelvis was found normal except for a patulous cervix. Curettage yielded two teaspoonfuls of large endometrial fragments. Twenty-five mg. of radium were inserted in the uterus for ten hours (filter of 1 mm. of brass and 0.5 mm. of silver). Menstruation since has been regular, lasting four to five days.

CASE 2 (L. I. C. H., 1919, No. 1408).—Primary menorrhagia followed by metrorrhagia; curettage unsuccessful; relief for three years following radium; recurrence, controlled by second dose of radium.

Miss H. F., aged seventeen years, was admitted to Dr. Polak's service at the Long Island College Hospital Sept. 17, 1919. Menstruation began at fifteen, occur-

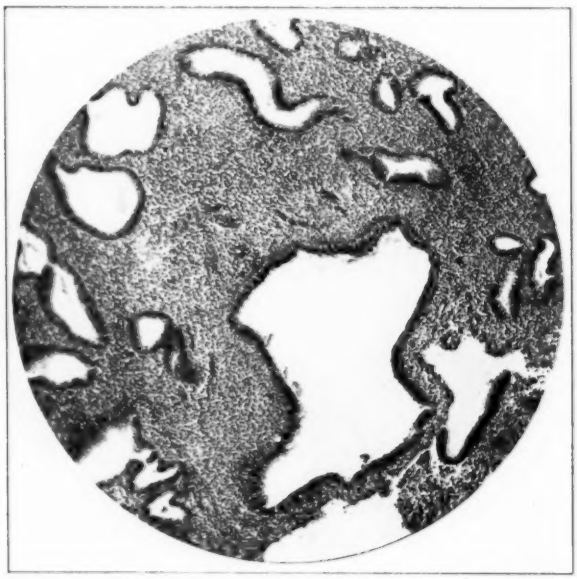

Fig. 1.—(Case 1.) Note hyperplasia of glands and stroma. The huge glands are noteworthy of endometrial hyperplasia.

ring twice each month for seven to eight days for the first year, then every two to three months until six months before. Since that time patient bled daily. A curettage two months after onset did not relieve the bleeding. Hemoglobin was 80 per cent. General physical examination was normal. Under anesthesia the uterus was found soft and enlarged, with the cervix patulous. A large amount of polypoid endometrium was removed. Radium dose of 250 mg. hours was administered through a filter of 1 mm. brass and 0.5 mm. silver. Until September, 1922, periods came every twenty-eight days, four days' duration. At that date, metrorrhagia recurred and continued daily until January, 1923. A second treatment of radium of 400 mg. hours through 1 mm. of brass and 0.5 mm. of silver, resulted in the return to a normal cycle to date.

CASE 3 (L. I. C. H., 1919, No. 1537).—Severe initial metrorrhagia requiring curettage and transfusion. Persistence of menorrhagia followed by metrorrhagia; control and cure by radiation.

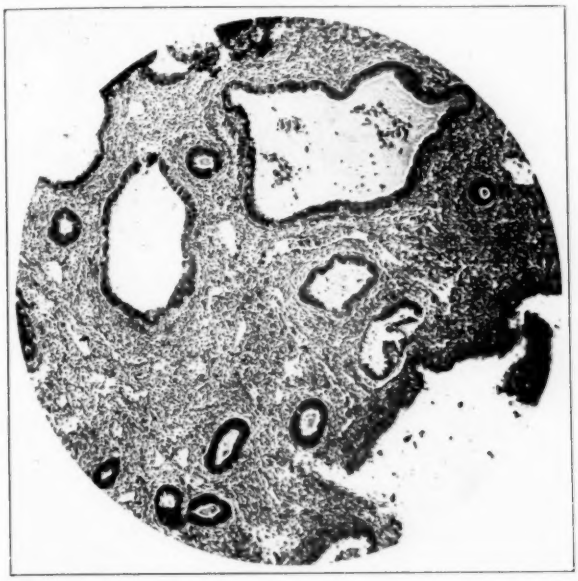

Fig. 2.—(Case 2.) Stroma and glands are hyperplastic. The cyclic pattern has been lost, huge glands are prominent. Note the large numbers of injected capillaries.

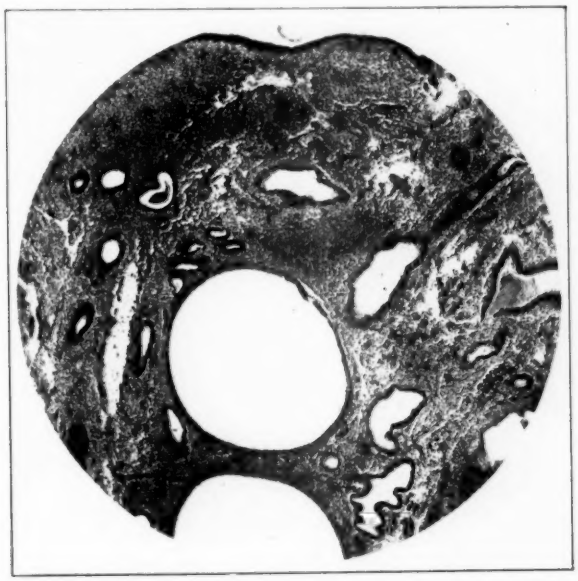

Fig. 3.—(Case 3.) Capillary congestion, glandular and stromal bleeding are all prominent. Note the huge circular glands typical of endometrial hyperplasia.

Miss E. D., aged thirteen years, was admitted to Dr. Polak's service February 22, 1919. The first menstruation began April 25, 1917, and continued very profusely. Because of severe anemia a curettage was performed ten days after the onset, followed by transfusion. Periods recurred in August, October and November of 1917, ceasing only after "injections" given by her physician. No further

bleeding occurred until May, 1918. Since that date, periods have been profuse, lasting seven to twenty days, always requiring medical intervention. Last period began February 10, 1919, and continued uninterruptedly until February 22. Hemoglobin was reduced to 32 per cent and red blood corpuscles to 1,980,000. Coagulation time was six and one-half minutes. A transfusion of 200 c.c. was given and the bleeding gradually ceased February 29, but recurred more severely on March 27. The patient was readmitted March 31. As previously, physical and pelvic examinations were negative. At operation the cervix was patulous and polypoid masses of endometrium were removed by the curette. A 600 mg. hour treatment of radium was given (filter 1 mm. brass and 0.5 mm. of silver). In April and May, periods lasted six days and the flow was moderate. From June 30 to July 5 bleeding was severe but responded rapidly to medication. To date, periods recur regularly and last four to six days; the quantity is normal.

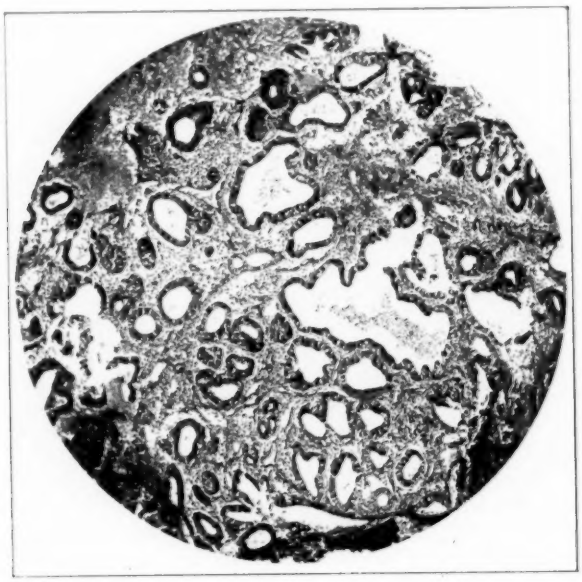

Fig. 1.—(Case 4.) Glandular hyperplasia is prominent. Stroma is congested and edematous. Typical changes of endometrial hyperplasia.

CASE 4 (L. I. C. H., 1922, No. 264).—Initial oligomenorrhea, followed by metrorrhagia; failure of curettage, relief by radium.

Miss E. B., aged twenty years, was admitted to Dr. Polak's service January 14, 1922. Menstruation began at eleven, periods following at two to four month intervals. Three years before, bleeding became continuous, spotting occurring from day to day. Curettage two years before relieved the bleeding for only one month. On admission hemoglobin was 70 per cent and physical and pelvic examinations were normal. A diagnostic curettage revealed a cavity 7.5 cm. in depth; the curettings were abundant and composed of large flakes of endometrium. A 600 mg. hour dose of radium was given (filter 1 mm. brass and 0.5 mm. silver). To date menstrual cycle is normal, the flow lasting two days.

CASE 5 (G. M. H., 1920, No. 2809).—Normal menstruation for one year after onset; menorrhagia, metrorrhagia, curettage unsuccessful, cure by radium.

Miss J. A., aged fifteen years, was admitted to Dr. Bailey's service at the Gen-

eral Memorial Hospital, August 10, 1920. Menstruation began at thirteen and continued regularly until October, 1919. From this date periods lasted thirty to forty-five days with a two to three day interval between. Curettage five months before was unsuccessful. Last period began July 16 and continued to date of admission. General physical examination was negative. Pelvic examinations showed a soft patulous cervix with an enlarged retroverted uterus. Curettage yielded old blood clots and large amounts of endometrium, evidently from the left lateral wall. Radium treatment of 500 mg. hours of emanation was given (filter 1 mm. platinum). Since September, 1920, periods have been regular and of four day duration, except for a transient amenorrhœa from April to August, 1921.

Case 6 (G. M. H., 1922, No. 6183).—Normal menstruation for two and one-half years, menorrhagia followed by metrorrhagia; curettage unsuccessful. Laparotomy. Cystic right ovary resected without result; improvement by radium.

Fig. 5.—(Case 5.) Stromal and glandular hyperplasia is marked. Note the congested capillaries coursing parallel to the surface. Interstitial bleeding is prominent and due to rupture of the vessels.

Miss H. B., aged seventeen years, was admitted to Dr. Bailey's service November 18, 1922. Menstruation began at fourteen, regular every twenty-eight days and of four to five days' duration. In April, 1921, menstruation continued for four weeks. In July the condition returned and lasted three weeks. Last period began November 5 and continued without let-up. On December 17 her physician noted "an enlarged uterus with a soft patulous cervix." There was no response to endocrine therapy and on January 7, 1922, a curettage was performed. The curettings were abundant and the pieces large. A soft projection on the left anterolateral wall gave the impression of a submucous fibroid. Following laparotomy January 16, no fibroid could be found. The right ovary was enlarged and cystic; the large cyst was accordingly resected and the smaller ones punctured. The uterus was suspended. There was no relief from bleeding except for an occasional three to five day period. On admission in November, 1922, the patient had been bleeding for ten consecutive weeks.

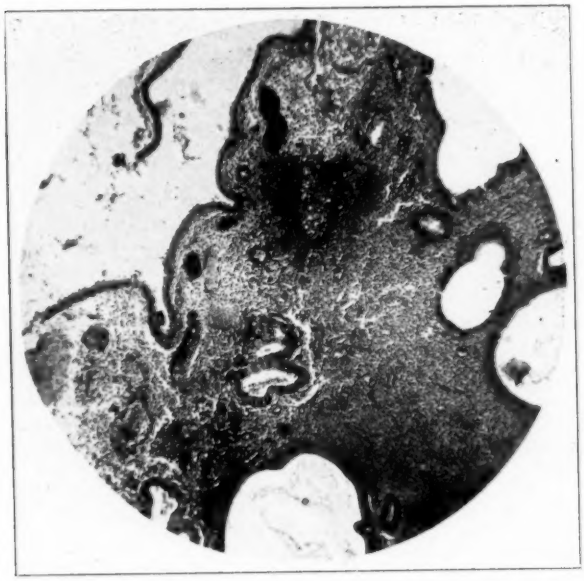

Fig. 6.—(Case 6.) Large hypertrophic glands are prominent in the dense hyperplastic stroma. The subepithelial capillaries are engorged; interstitial bleeding is prominent.

Fig. 7.—(Case 7.) Thrombi in the vertical capillaries (*c*). Necrosis has occurred and the superficial layers of the endometrium are being detached. Glands are huge and the lining cells hypertrophic. Stroma is hypertrophic.

Physical examination was negative. The pelvis was normal and the uterus anterior. Curettage again revealed hypertrophic endometrium. A dose of 445 mg. hours of radium emanation was given (filter 1 mm. platinum). To date, patient menstruates every month for six days but quite profusely.

CASE 7 (L. I. C. H., 1924, No. 3074).—Attacks of menorrhagia and metrorrhagia since onset; abnormality in uterine development; control of symptoms by radium.

Miss M. S., aged nineteen years, was admitted to Dr. Polak's service on May 7, 1924. Menstruation began at fourteen and recurred every two weeks, the flow lasting for ten days, so that the patient was practically never free from bleeding until the age of sixteen. At this time, menses recurred every twenty-eight days and lasted for three days. Between the ages of sixteen and seventeen bleeding was constant. Until three months prior to admission menstruation followed every twenty-eight days for fourteen days. Since then her periods have again become prolonged lasting twenty-one days. Last menses began April 26 and continued to date of admission.

Physical examination was generally negative except for a moderate secondary anemia (Hb. 70 per cent). Rectoabdominal examination revealed a soft cervix of puberty; uterus was anteflexed; a tuboovarian mass filled the left vaginal fornix. Laparotomy was performed on May 9. Uterus bicornis unicollis was found; the right tube was normal; the ovary held moderate numbers of follicular cysts. The left tube was clothed with adhesions; the ovary was the seat of chronic perioophoritis. Left salpingo-oophorectomy was done. After closing the abdominal wound, the double uterus was curetted and 25 mg. of radium inserted in the right horn for sixteen hours. Dose 400 mg. hr. (filter 1 mm. brass, 0.5 mm. silver). The curettings were abundant, thick and hemorrhagic. Since operation menses have recurred regularly every twenty-eight days for three days.

With the picture of prolonged and profuse bleeding as presented by the above histories, the cause is naturally carefully searched for in the uterus.

PATHOLOGY

It will be recalled that in three instances the uteri were large on palpation and in two others enlargement of the organ was determined by measurement. In the other 19 cases the measurements were not noted, but, as all uteri were sounded before curettage, it is reasonable to assume that any marked departure from normal would have been noted. In all instances the curettings were abundant, and the large size of the fragments noteworthy. A polypoid character was noted in three cases.

The abundance and size of the fragments is explained by the microscopic picture which is almost strikingly uniform in all cases. The details are shown in the accompanying microphotographs.

Many of the endometrial fragments are polypoidal and lined by single or multiple layers of hypertrophic epithelium. The remaining fragments are generally thickened. All changes are the result of hyperplasia of the component endometrial structures. The glands are increased in size and numbers. As a rule the cyclic pattern is lost and the glands are irregularly arranged and distributed. There is no recognizable division into a surface, glandular and basal zone as typical of a normal mucosa in the late interval and premenstrual stages. In form, the glands vary considerably. Though most are round or oval, branched and saccular forms are not infrequent. Huge circular glands are prominent and universally found; they are not cystic, as evidenced by the tall columnar cells. As a rule a single layer of columnar cells is found in the glands, but multiple layers (2-6) are not infrequent. The cells are huge with abundant cytoplasm and are almost filled by large, oval hyperchromatic

nuclei. Areas where the glands are within normal size, and regular in form, show the pathologic deviation by contrast of the tall columnar cell with its huge nucleus against narrow lumen. These glands are rather frequent in small polypoid fragments evidently of surface origin. The lumena frequently contains secretion or red blood corpuscles. Secretion is not uniform and adjacent glands of the same endometrium are without secretory collections.

The stroma, like the gland tubules, is universally hyperplastic. Though the cell bodies could not be sharply defined, the enlarged oval, round or fusiform nuclei are indicative of hypertrophy. Mitotic figures are not infrequent and are indicative of cell multiplication. Contrasted to the gland hyperplasia the quantitative ratio is not constant. Glands as a rule show relatively greater hyperplasia. Foci of interstitial hemorrhage often compact beneath the surface epithelium, are a frequent finding. Edema is universally present and accounts in part for the increased thickness of the mucosa.

The vascular changes are especially noteworthy. Capillaries are greatly increased in size and numbers and are generally engorged. Perpendicular loops predominate, though parallel loops beneath the surface epithelium are often seen. Many have ruptured with resulting interstitial hemorrhage, at times so intense as to open directly on the surface. As a rule, however, this is only of sufficient intensity to cause atrophy of the lining epithelium. Thrombosis of the capillaries is occasionally seen both near the surface and in the deeper zones of the endometrium. The significance of this finding will be emphasized in the following paragraphs. Sclerotic venules or arterioles are not infrequent.

In brief, these features of diffuse endometrial hyperplasia are identical with those in the menopausal group. R. Meyer suggests the basal layer as the earliest seat of the lesion.

Since the mucosa alone is insufficient for a complete detailed study, recourse was had to the literature for the condition of the myometrium. The advent of radium has eliminated hysterectomy so that pathologic material is scant. Although many studies include the menopause type and are not strictly applicable, yet these findings are of interest.

Theilhaber and Meyer describe fibrous hyperplasia with muscle replacement so that control of the blood vessels by the latter is lost. This is assumed as the cause of bleeding. Reinicke has noted atheromatous changes in the blood vessels. More recently William Fletcher Shaw[1] has divided the uteri of chronic metritis into two groups: (1) Subinvolution; (2) Hypertrophy. In both of these glandular hyperplasia occurs, with additional changes throughout the uterine wall. To the subinvolution group belong the uteri of multipara with menopausal hemorrhage. Expanding Goodall's[2] studies of involution of the puerperal uterus, Shaw emphasizes the persistence of the elastic intima of the old vessels during puerperal involution; and normally, scant trace is left of the old intima. This persisting elastic tissue interferes with contraction of the muscle wall of the new vessels. In addition there is increased fibrous and elastic tissue throughout the myometrium. A personal study of many uteri of women dying of extrapelvic disease in the fourth decade would indicate these changes as incidental rather than causative, for no bleeding was present. The hypertrophic group includes uteri of virgins and nullipara. The majority suffer from menorrhagia and dysmenorrhea from puberty with a gradual increase in severity. "The endometrium shows a marked increase in gland and stroma as the

primary event. This is followed by a work hypertrophy of the myometrium causing an enlargement of the organ. The ratio of muscle to fibrous tissue remains normal.'' His microphotographic reproductions of sections stained by the Weigert-van Gieson methods are very interesting.

An older study by Pankow[3] contradicts these findings. This author studied 52 uteri removed for bleeding, using for control uteri removed for prolapse, without history of hemorrhage. Uteri of two virgins and one nullipara are included. Gross comparison and careful study of sections following the Weigert-van Gieson stain failed to reveal any essential difference in the myometrium of both groups, though hyperplastic endometrium was often encountered in the bleeding parous uteri. Yet, the control group is open to question, for passive congestion which goes hand in hand with prolapse could induce similar pathologic changes and hence deductions need be carefully made. Kajii[4] also reports in bleeding uteri the ordinary structure of a multiparous uterus. Faced with this maze of contradiction one readily appreciates Aschoff's compromising term of metroendometritis. Yet it must be emphasized that all observers note endometrial hyperplasia, even after Hitschman and Adler[5] have differentiated the premenstrual mucosa from the true pathologic hyperplasias.

Ewing[6] in discussing adenomata and adenomatoid conditions notes such proliferative changes in the wake of the following factors: (1) prolonged irritation; (2) accentuated repair following trauma; (3) increased response to excessive physiologic function. Certainly in the puberty group, trauma inflammation and parity are excluded, leaving ''response to excessive physiologic stimulation as the exciting factor.'' The ovary has long been known as the cause of the cyclic hypertrophy of the endometrium.

In 1906 Hitschman and Adler first demonstrated the cyclic changes in the uterine mucosa. Subsequently these were formulated with the stages in maturation of the graafian follicle, ovulation and corpus luteum formation. The details need not be given. For our purposes it suffices to note that beginning enlargement of uterine glands coincides with ripening of the follicle, proceeding at a greater momentum with the formation of the corpus luteum and reaching the ''pregravid'' state at the heighth of development of the corpus. Death of the ovum is followed by involution of the lutein body and in turn by ''desquamation of the pregravid endometrium or menstruation. During development of the corpus luteum ripening of other follicles is inhibited.

Correlation between ovary and glandular hyperplasia of the uterus has been shown experimentally. Lauth[7] has produced in animals the pathologic changes of ''metroendometritis'' by injection of ovarian extract. Schiller[8] in sexually premature rabbits produced the condition of heat with its associated hypertrophy and hyperemia of the uterus, by injections of corpus luteum. More recently Frank and Gustavson,[9] using the fatty residue from follicular fluid, corpus luteum and placenta, caused hyperplasia and hyperemia of the müllerian tract and mammae. In virgin immature rabbits and guinea pigs extracts from follicular fluid cause hyperplasia of the uterus, vagina, and breasts. The ''female sex hormone'' has been isolated from the blood of the sow and shown present in greater quantity during estrum. Allen, Pratt, and Doisy,[10] using liquor from human ovaries obtained by operation, have produced functional hyperplasia in rats, as shown by the vaginal spread test. Corpora lutea and placenta contained a similar hormone. From the functional standpoint similarity in function of follicle and corpus luteum must be greatly emphasized. Evans[11] has further shown prolongation of vaginal proliferation (indicative of estrum and hyperplasia) in rats, where the ovaries contained multiple ripening follicular cysts and absence of corpora lutea.

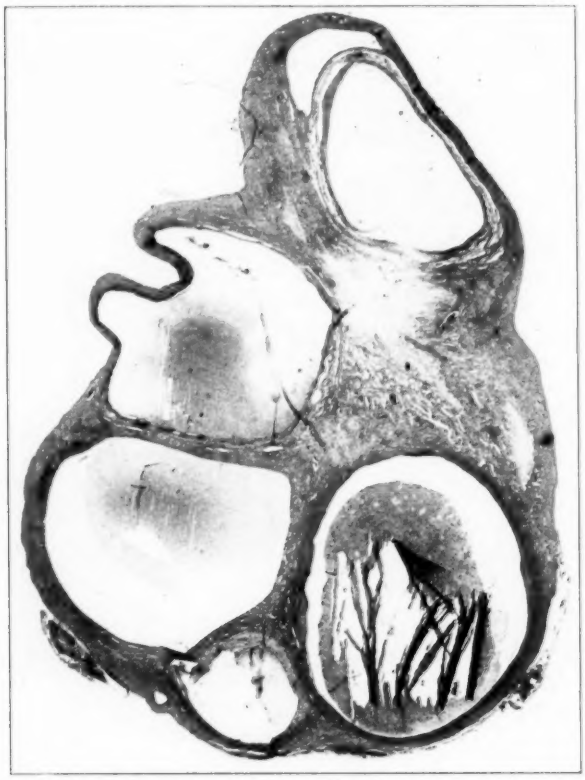

Fig. 8.—(Case 7.) Section transversely through the lower pole of the ovary. The organ is practically completely filled with follicular cysts.

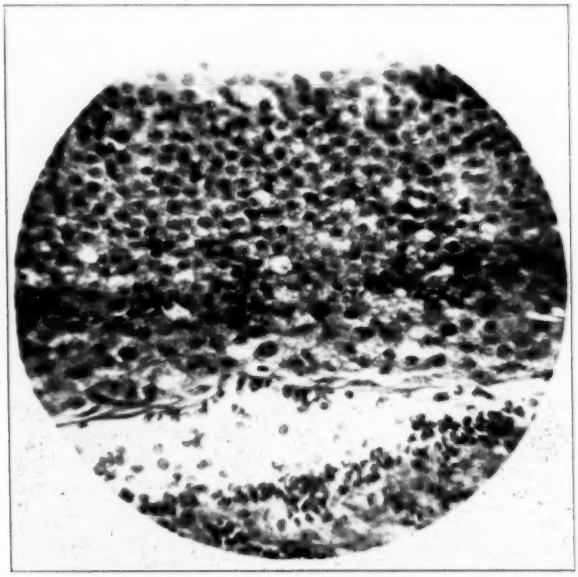

Fig. 9.—(Case 7.) Hypertrophic granulosa cells forming the lining of the follicular cysts noted in Fig. 8.

This is practically in accord with many observations on human ovaries.

Clinically Lauth[7] reports small cystic degeneration in one or both ovaries removed by panhysterectomy for bleeding. Franz[12] in an older publication notes follicular degeneration and ascribes the increased number of atresic follicles to fibrosis and reduction in the number of blood vessels. Similar findings are reported by Gottschalk, Winternitz and J. Veit. Kajii also emphasizes cystic follicles in the ovary. Cystic changes are recorded by S. H. Geist[13] in four multipara with "essential bleeding." Ludwig Adler[14] reports a case in a twenty-year-old virgin essentially similar to case 6 of our series. Uterus and adnexa were removed. Both ovaries were converted into numerous follicular cavities, no corpus luteum was present. Microscopically there were numerous cysts and atresic follicles varying greatly in their stage of ripening, and presenting a striking growth of granulosa cells. A corpus luteum was not found. Robert Meyer[15] recognizes a group of "cystically degenerated ovaries" associated with the history of bleeding and hypertrophy of the endometrium. These show several large follicles with normal or slightly proliferating cells, and also cysts in the regressive stage; at times lined by an unusually marked theca lutein layer. None of the follicles reach development but persist, even after death of ovum. Persistence of follicles causes a summation of stimuli to the uterine mucosa which is prolonged and constant. Corpus luteum formation is absent. Schroeder[16] reports similar findings but interprets the changes as due to persistence of multiple follicles ripening simultaneously, since inhibition is not exercised in the absence of corpus luteum. Novak and Martzloff,[17] however, report recent and functioning corpora in their studies in addition to large numbers of follicular cysts, and suggest this change for cases in which menorrhagia is the predominant clinical symptom.

In our series only one ovary is available for study (Case 7). Though allowing no deductions, it presents cystic changes as recorded by other observers. (Figs. 8 and 9.)

The organ is ovoid in form and measures 3 x 2.5 x 2.5 cm. Its anterior surface is clothed with fairly firm injected adhesions. The surface is lobular, due to the presence of numerous cysts, bulging beyond the cortex; these varying from 3 to 10 mm. in size. Most are translucent; the smaller ones, however, are bluish and hemorrhagic. Round yellow streaks, irregularly distributed, show remnants of involuting corpora lutea. On gross section the interior of the ovary is completely cystic. Narrow stromal strands separate multiple cysts. These vary from 5 to 12 mm. in size and fill cortex and medulla. Several are hemorrhagic or show zonal hemorrhage externally. Bleeding is present beneath the adhesions noted anteriorly.

Multiple sections of the ovary reveal similar structural changes. The germinal layer is poorly preserved. Vascular adhesions line the anterior surface. The tunica is sclerotic. Cortex is normal and holds exceedingly large numbers of primordial follicles. Moderate numbers show enlarged hydropic and degenerating ova. Others had just begun maturation when degeneration occurred, so that solid clusters of granulosa cells surround the dying ovum. In others liquor folliculi had appeared. The predominant change, however, lies in the numerous cysts. The majority retain the granulosa layer despite their size. In foci the layer is hypertrophic and 12 to 18 layers are present. In some cysts large areas present these changes. Subjacent lies a broad zone of large theca interna cells; a narrow layer of fibrous stroma separates the cell layers. In some follicular cysts granulosa cells have disappeared and only the theca cells persist. The vessels about the cysts are injected. In foci several have ruptured with zones of stromal hemorrhage; in many this has followed into the cavity. A few corpora albicantia are seen. These are large and fairly recent. A regressing corpus with shrunken fatty cells and pycnotic nuclei is also seen. Beneath the adhesions endometrial implants are seen. From a large

central cavity, secondary tubules are seen lying in typical endometrial stroma. The latter is filled with blood. Gland cells are tall, columnar, and ciliated. Hemorrhage into gland spaces has also occurred. The medulla of the ovary is largely occupied by cysts and shows no special changes from the normal. Blood vessels everywhere are numerous and conjested. The hilum of the organ shows normal vessels.

In brief, the changes are typical, and the ovary has been converted into multiple cystic spaces lined by granulosa cells and containing large amounts of follicular fluid. The potency of this substance in production of proliferative changes has been demonstrated by Frank and Allen and Doisy. The continued and prolonged stimulation from the follicle is the necessary factor converting a temporary or functional hypertrophy of the endometrium to a pathologic of permanent hyperplasia.

MECHANISM OF BLEEDING

Physiologically menstruation begins with involution of the corpus luteum, and it has been believed that the function of the corpus is the inhibition of menstruation. Halban and Köhler's[18] experiments in humans, causing the onset of bleeding within two to four days after cautery destruction of the corpus luteum, support this viewpoint. Seitz and Wintz[19] have shown similar effects upon ovaries exposed to radium, in which ripening follicles and young corpora lutea were damaged. Only when the corpus was at the height of efflorescence, however, did bleeding follow, and the effect was essentially desquamation of a pregravid endometrium following involution of the corpus. If ovarian pathology in endometrial hyperplasia excludes formation of the corpus luteum, as believed by Meyer, Schroeder and Seitz, uterine bleeding cannot be directly inaugurated by the ovary.

The clinical symptom of bleeding, however, is accounted for by the vascular changes in the hyperplastic endometrium. Adler,[14] R. Meyer and R. Schroeder[16] have found thrombosis in the endometrial capillaries. The adjacent mucosa becomes necrotic and during the separation of the slough and resulting ulcer formation, bleeding proceeds from the site of demarcation. In the twenty-six cases reviewed, these thrombotic changes were found only on two occasions in the curettings examined and hence cannot be considered as the predominant mechanism. Seitz[20] notes and emphasizes the dilatation and elongation of the endometrial capillaries, so prominent a finding in these series. The engorgement is a pathologic accentuation of changes noted by Mauthner[21] in the capillaries of a premenstrual mucosa. In this phase the terminal capillaries which run vertically through the mucosa, to aberrate next to the glands, are constricted, while the connecting loops parallel to the surface are wide and tortuous. In the postmenstrual phase, the vertical branches are dilated and the horizontal branches narrow. The persisting hyperplastic endometrium of essential bleeding may be considered the pathologic analogue of the hypertrophic premenstrual mucosa. It is reasonable, therefore, to find the capillaries engorged near the surface, as is so well demonstrated in the microphotographs. According to Seitz these rupture readily following mechanical insult. This is concomitant with many active body movements and changes of intraabdominal pressure, as coughing, sneezing, vomiting, etc. Severity of bleeding will depend upon the size and number of the vessels affected.

In sixteen of the curettings examined focal interstitial hemorrhage was present. In ten, this was marked and formed a compact zone beneath an atrophic and compressed surface epithelium, as shown in microphotograph. Separation of the necrotic area of surface epithelium and stroma reopens the congested vessels and permits free bleeding into the uterine cavity.

CONCLUSIONS

1. Puberty hemorrhage is a definite clinical entity presenting as a menorrhagia or metrorrhagia in the absence of inflammation, neoplasia or the pregnant state.

2. The soft patulous cervix is pathognomonic; the body may or not be enlarged.

3. Symptoms recur after curettage but are always controlled by radium.

4. Curettings are abundant, thickened and frequently polypoid. This is the result of a diffuse glandular, stromal and vascular hyperplasia.

5. Persistence of solitary ripening follicles or simultaneous maturation of multiple follicles accentuates a physiologic endometrial hyperplasia into a pathologic type. These changes have been experimentally reproduced by Frank and others in laboratory animals.

6. Corpus luteum formation is absent.

7. The uterus is the direct seat of bleeding. It results from thrombosis of the endometrial vessels and ensuing necrobiosis, and from actual mechanical rupture of engorged capillaries.

8. The factors inaugurating persisting, follicular cysts in the ovary with its concomitant endometrial hyperplasia, remain a subject for future study.

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THE NORMAL AND PATHOLOGIC PHYSIOLOGY OF PREGNANCY*

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REPRODUCTION represents the maximum of physiologic function of woman and, therefore, necessarily calls for the maximum of functional activity of all maternal tissues and organs. I say of "all organs," firstly, because today we accept as evident truth that all organs functionate as a harmonious unit under the controlling influence of a superimposed regulatory mechanism, and secondly, because during pregnancy all maternal organ function in the last analysis seemingly accrues to the benefit of the fetus in utero.

From this broader viewpoint it can easily be seen how likely confusion and error will result, and probably have resulted, from a method of study of the physiology and pathology of pregnancy which heretofore, in a rather onesided manner, was mostly directed towards investigating the behavior of but one organ (kidney, liver, thyroid, etc.), or ascertaining the changes in one organ system (vegetative nervous, endocrine, circulatory, etc.), or which tried to discover the one likely pathogenic factor (cytotoxin, foreign protein, placental ferment, or end-products of fetal metabolism).

A definite failure with merely anatomic-histologic investigations necessarily created keener interest in the study of functional deviations. Again in this respect, failure with testing organ function solely

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by means of chemic analysis of excretions has led to the development of newer methods which endeavor to gauge organ function more reliably by the chemic study of the retained body fluids. Such chemic analytic investigations today make use of all the latest advances in biochemistry and the physico-chemistry of colloids. Writers begin to speak of the molecular biology of pregnancy (Schade,[1] Seitz[2]). Thus, e.g., the interesting fact has been revealed that during normal pregnancy the definite and always constant proportional relations of sodium, potassium, and calcium contents and with it the ion concentration of the blood are altered. This, indeed, is an important discovery since it proves that pregnancy actually results in a constitutional change but—in contrast with changes of this kind outside of pregnancy—without disturbing a state of perfect health. This fact in itself convincingly demonstrates that however profound such alterations in the chemic constitution, morphologic condition, or functional activity of certain body fluids, tissues and organs are, the equilibrium in general still is maintained—of course, only through propitious modification in the work of that superimposed regulatory mechanism which controls all individual organ function as well as harmonious organ interaction.

An appropriate conception of the physiology of pregnancy then is not directly dependent upon accurate information concerning morphologic, chemic, or functional alterations observed during normal pregnancy in this or that of the maternal organs but rather on the understanding of the underlying causes and of the presumably rational purpose of all these alterations.

RELATIONS OF THE PHYSIOLOGY OF PREGNANCY TO THE PHYSIOLOGY OF MENSTRUATION

Of the many general changes, commonly, if not regularly, seen in normal pregnant women, often at the very beginning of gestation, I shall first mention one group for which, in my belief, we must recognize cyclic ovarian activity as the one common underlying cause.

Blood Pressure.—While we cannot speak of a physiologic rise of blood pressure during pregnancy, a striking variability with occasional marked temporary rise is a practically constant symptom. Even persistent hypertonia can occasionally be observed in the absence of any of its known causes (Huessy,[3] Kehrer[4]). In view of the physiologically increased work of the heart, expressed in an increase of both the contraction volume and blood output per minute (Frey,[5] Weiss[6]) and in a greater amplitude of the pulse pressure (Slemons and Goldsborough[7]), the maintenance of the blood pressure, approximately at a normal level, is determined by changes in the tonus of the capillaries. Therefore, a more or less physiologic rise might be

caused by the common angiospastic states of the capillaries (Hinselmann[8]), due to alterations in the entire vegetative nervous system and especially the vasomotor system during pregnancy.

Basal Metabolism.—An increase of the basal metabolic rate is a characteristic phenomenon of pregnancy (Baer,[9] Cornell,[10] Harding,[11] Haselhorst and Plaut,[12] Huessy,[3] Klaften,[13] Knipping,[14] Root and Root,[15] Rowe, Alcott and Mortimer,[16] Sandiford and Wheeler[17]). This increase often manifests itself in a slight rise of temperature and in faster respiration (Huessy).

Carbohydrate Metabolism.—The reduction during pregnancy of the ability to assimilate carbohydrates and even starch, when taken in large doses—manifested in a glycosuria—is now well known (Ehrenfest[18]). This phenomenon evidences itself so early in pregnancy that various diagnostic tests of pregnancy have been based on this apparent sugar intolerance. The dependence of this metabolic alteration upon ovarian function is firmly established (Kuestner[111]).

Protein Metabolism.—Definite deviations from normal have been ascertained in the protein metabolism of pregnant women. Protein disintegration in the earlier stages of gestation is characterized by a reduction in the excretion of urea with a relatively high ammonia elimination in proportion to the total nitrogen. Also the amino-acids and polypeptides in the urine are increased (Falk, Hesky, and Zangemeister, quoted by Huessy). However, late in pregnancy, with the same nitrogen intake, less nitrogen and less urea are excreted on account of nitrogen retention (Hoffstroem, Slemons, Zuntz).

Thyroid.—Enlargement of the thyroid early in pregnancy, associated with increased thyroid function, is today a generally admitted fact.

Vegetative Nervous System.—There exists general agreement that during pregnancy the entire nervous system is in a state of increased irritability. In regard to alterations of the vegetative nervous system, writers disagree as to whether these changes express themselves more in the form of a vagotonia or a sympathicotonia (Louros[19]), but no doubt is left concerning the fact that such changes occur. They are necessary for a required change in blood distribution (Huessy) and are evident in the existing modification of metabolism (Seitz[20]), of endocrine function or of the secretory activity of many organs. Careful pharmacodynamic tests show, however, that it is unjustifiable to ascribe every mysterious or puzzling phenomenon of pregnancy simply to a vagotonia or a sympathicotonia (Peyser[21]).

Respiration.—The respiratory rate as a rule rises early in pregnancy and therefore this change cannot be due to a decrease in the vital capacity of the lungs, obviously so, because even late in pregnancy a change in the configuration of the thorax usually brings full

compensation for the elevation and restriction in the respiratory movements of the diaphragm (Kehrer[4]).

Blood.—Of the many and marked alterations in the blood of pregnant women I will mention in this connection only the following: Often a leucocytosis is encountered (Heyn,[22] Huessy, Kehrer) and changes noticed in the erythrocytes which indicate an hyperactivity of the hematopoietic system (Umber). A lowering of the carbon dioxide combining power has been almost universally recorded (Killian and Sherwin,[23] Marrack and Boone,[24] Wesselow and Wyatt[25]). The fixed acidity of the blood is physiologically increased during pregnancy (Hasselbach and Gammeltoft, Rowe, Banks and Alcott,[113] Wieser,[26] Williamson[27]). However, it is important to realize that the characteristic tendency of pregnant women to acetonuria, especially in the presence of vomiting or with a reduction of the carbohydrate intake (Harding and Duncan), represents quite a different type of acidosis, though the one might be superimposed on the other or be even related to it (Cook[28]). The concentration of the acetone body contents of the blood is normally increased in pregnancy, markedly so in almost all types of so-called toxicosis (Bokelmann and Bock[29]). This disturbance of the acid base equilibrium possibly plays an important rôle in sudden shock or even death after obstetric operations (Williamson[27]). The recovery of such patients under appropriate treatment, when the combining power has dropped within or even below the so-called fatal zone, only demonstrates the remarkable effectiveness, also during pregnancy, of that automatic mechanism which controls the ion concentration of the blood.

The common occurrence of acetonuria probably is due to an inability to burn up all fat and, therefore, as in the diabetic patient, manifests itself promptly after reduction of the carbohydrate intake. This striking disorder of metabolism appears so early that it has been made the basis for a diagnostic test, useful within a week after nonappearance of the expected menstruation (Pritzi and Lichtmann[30]).

All investigators concur in the fact that during pregnancy a hydremia exists (Harding[11]), starting probably with the onset of pregnancy and certainly being well marked already in the third month (Plass and Bogert[31]).

The biochemic and functional alterations which I have so far mentioned are so commonly observed in pregnant women that rather generally they are thought to represent typical and characteristic changes caused by pregnancy itself. I believe that this view is untenable because they all, as I will presently show, have been found to be equally as common and typical in the premenstrual state.

Considering only extragenital phenomena which in normal healthy women are observed during the week preceding the menstrual flow,

I can mention the following: A rise in blood pressure (Amos[32]), often a slight rise in temperature and pulse rate (Hafkesbring and Collett,[33] Cullis, Oppenheimer and Ross-Johnson[34]), and increased metabolic rate (Labhardt and Huessy,[35] Lanz,[112] Snell, Ford and Rowntree,[36] Wakeham[37]), an alteration in the carbohydrate metabolism expressing itself in lowered sugar tolerance (Heilig,[38] Kuestner,[39] Umber,[40] and others), and increase of size and function of the thyroid gland (Weidemann), certain disorders of the vegetative nervous system manifesting themselves chiefly in the form of a vagotonia (Franke[41]), the latter expressing itself also in abnormal behavior of the gastrointestinal tract when studied roentgenologically after a barium meal (Ludlum and McDonald Ellis[42]). Periodic changes with menstruation in the sensibility of the secretory and vasomotor nerves have been ascertained by pharmacodynamic investigations of the vegetative system (Dahlmann[43]). Monthly variations in cardiovascular activity and respiratory rate have been recorded (Moore and Cooper[44]). Circulatory and structural alterations of the capillaries are not limited to the capillaries of the endometrium, as is proved, e.g., by reports of ecchymoses on both thighs (Hirschberg[45]) or of bloody secretion from both mammillae recurring regularly with each menstruation (Zadik[115]). We can speak today of characteristic alterations of the physicochemic constitution of the blood in relation to menstruation, pertaining to the number of erythrocytes (Gumprich) and leucocytes (Dirks, Hofstetter[110]), to carbon dioxide combining power (Kuestner), disturbance in the acid base balance (Weismann-Netter[46]), its water and salt contents (Heilig[47]) and even to its calcium concentration (Malamud[48]). During the seven days preceding menstruation, exactly as in early pregnancy, there exists a marked rise of the urinary ammonia coefficient, due to a rise of the total output of ammonia rather than to a decrease in the total output of urinary nitrogen (Bond[49]). Menstruation apparently increases the permeability of the meninges (Heilig and Hoff[50]), and this same change has been found in pregnant women (Benda[51]), a condition which might account for mental disturbances noticed at times in menstruating as well as in pregnant women. Most significant in its possible bearing on the complex and still little understood problem of toxemia of pregnancy, in my opinion, is the fact that a heretofore merely superstitious belief of the laity in menstrual toxins now has been placed on a firm scientific basis (Schick,[52] Macht and Lubin[53]), though it is possible that their evident inhibitory effect on yeast fermentation not necessarily proves the existence of a specific menotoxin since this effect might be due only to an excessive secretion during menstruation of such substances as cholin or creatinine (Polano and Dieti[54]). Of great interest in this connection must also

prove the observation that premenstrually the blood exhibits a marked increase of proteolytic ferments and that, therefore, at that time the blood often gives a weakly positive Abderhalden reaction (Kjaergaard[55]).

That such manifold and profound chemic and functional changes occur with menstruation should not be surprising. We look upon them today as essential and characteristic features of the physiology of menstruation. We admit as established fact that this cyclic wave during a woman's menstrual life, first suggested by Jacoby, of New York, in 1876, and two years later strongly supported by Goodman, of Louisville, actually exists. We know that these waves are the general manifestations of cyclic changes in ovarian activity, that each wave rapidly approaches its peak during the premenstrual week, then abruptly drops and remains at its lowest level in the intermenstruum.

This similarity, if not identity, of premenstrual systemic changes with those so far quoted as typically observed usually early in pregnancy, is striking and suggestive but as a matter of fact it is only something that we should expect as natural. All changes occurring regularly with the discharge of an ovum from a matured graafian follicle necessarily are entirely independent from the fact whether this discharged ovum later is fertilized or not. These changes, therefore, must be in evidence when fertilization has taken place and the fertilized ovum has reached the uterine cavity.

We thus conclude, first, that systemic changes noticeable at the beginning of pregnancy and identical with those of the premenstrual state are not caused by pregnancy itself but are dependent upon a certain phase of the ovulation process and are produced by ovarian hormones, and secondly, that, in accordance with our present views concerning menstruation, general systemic changes exactly like those in the uterus and breasts express the monthly preparation for impregnation.

CHANGES DUE TO ADAPTATION TO FETAL REQUIREMENTS

Unlike the corpus luteum of menstruation, however, that of pregnancy persists. Its hormonic influence during the progress of pregnancy is supported and finally continued by placental hormones which have been found chemically and physiologically identical with those of the corpus luteum (Herman, O. Frankl,[56] R. T. Frank). Therefore, with the onset of pregnancy, i.e., with the realization of the merely anticipated implantation of a fertilized ovum, the premenstrual changes of uterus, breasts, and almost all other organs will persist, but necessarily in an intensified or otherwise modified form. We might say that systemic changes, in the premenstrual state expressing solely certain *qualitative* requirements of pregnancy, later adapt themselves to actual *quantitative* needs.

A gradual, more or less complete, adaptation of certain biologic premenstrual changes to quantitative needs arising in the course of pregnancy can be easily demonstrated by a few examples.

The *hydremia* of pregnancy seemingly exists at the very beginning of pregnancy (Plass and Bogert[31]). It thus cannot be the result of disturbed renal function as often is claimed. More reasonably it can be looked upon as preparation for, and adaptation to, fetal needs, since within a comparatively short time his dry substance contents are lowered from 95 to 75 per cent (Wieser[26]). As another reserve supply for water needs created by pregnancy can be regarded the commonly present edema of pregnant women. Also very marked edema is seen in the absence of any renal disturbance (Eckelt, Vollhard). As a matter of fact all connective tissue, not only the subcutaneous, contains more fluid and to this is due the characteristic and advantageous softening of such structures as vagina or pelvic ligaments (Kehrer[4]). This characteristic readiness for the formation of hydropic conditions during pregnancy is generally acknowledged and expressed by different writers in such terms as "latent tissue hydrops" (H. Strauss), "preedema" (Widal), or "edema preparedness—*Oedembereitschaft*" (Zangemeister).

The *basal metabolic rate* rises with the progress of pregnancy until it amounts, near term, on an average to above 16 per cent (Klaften[13]). Marked rise occurs both in the total twenty-four hour calories and in the calories per unit of weight during the later months of pregnancy (Root and Root[15]). The total heat production late in gestation amounts finally to 25 per cent increase of total calories for each hour as compared with conditions ascertained before impregnation in the same individual. The energy production of unit mass of the mother's protoplasmatic tissue remains practically unchanged throughout the course of pregnancy, and the increase in the total heat production thus in the main is due to the increasing mass of fetal protoplasmatic tissues (Sandiford and Wheeler[17]). This readily explains why the actual increase of the metabolic rate is disproportionate and comparatively too high in comparison to the mother's weight increase. The fast growing fetus obviously has a higher metabolic rate than the mother. A total weight increase of the pregnant mother, amounting up to six weeks before term to only 14 per cent, is found associated with a 23 per cent rise in the metabolic rate (Root and Root[15]).

To provide the required 35 to 40 additional calories per kilogram bodyweight (Magnus-Levy), all metabolism has to be speeded up, and especially that of the carbohydrates, which represent by far the largest part of the total food intake. This speeding up of sugar assimilation accounts for the common glycosuria after the intake of large amounts of sugar as result of a protective lowering of the renal

threshold for sugar to prevent a hyperglycemia (Ehrenfest[18]). This phenomenon might be emphasized as a good example showing how a physiologic change of the premenstrual state as the result of its adaptation to quantitative needs of the fetus at least temporarily will give rise to a symptom which in every nonpregnant individual is indicative of a truly pathologic condition. The effort at adaptation, here like in other and especially in pathologic-physiologic conditions, actually results in a surplus of function.

On the other hand we find that such an evident effort at adaptation to increased demands, at least temporarily might prove insufficient, as often can be observed in relation to the *calcium metabolism* during pregnancy.

An initial typical increase of the calcium concentration of the blood is almost invariably followed late in pregnancy by a marked decrease (Krebs and Briggs,[58] Plass and Bogert,[59] and others). It is a well-known fact that in a normal, healthy individual the Na, Ka, Ca relations of the blood are fairly accurately maintained in the proportions of 100 : 2 : 2, but during pregnancy a shift occurs in favor of calcium (Seitz,[60] Schade[1]). The calcium needs of the fetus are known. The quantity daily retained by him amounts to more than 600 mg. (Widdows[61]). But a surplus of calcium is also deposited in the form of osteophytes, chiefly on the inner surface of the mother's cranium, or on the maternal surface of the placenta. We, therefore, can understand why at the moment of delivery the maternal blood always shows a markedly lower calcium concentration than the fetal blood (Hellmuth[62]).

If the calcium intake with the food is inadequate, or, as it is more likely, if parathyroid function is inadequate, a negative calcium balance will result. Recently much clinical and experimental evidence has been furnished to prove that there exist very intimate connections between the potassium and calcium concentration of the blood and various clinical pathologic conditions, especially derangements in the function of nervous and endocrine systems (Seitz,[2] Zondek[63]). It has been ascertained that the Chvostek facialis phenomenon, which in its marked form is accepted as a characteristic sign of tetany, to a slight degree can be elicited in about 75 per cent of all pregnant women (Kehrer). Intravenous injection of calcium stops in pregnant women typical attacks of true tetany (Kehrer). Calcium deficiency, rather than chemic changes in saliva, is today generally looked upon as the main cause for the frequent destruction of teeth by caries during pregnancy. All these facts support the view that during gestation the calcium metabolism, though evidently speeded up, at times still remains quantitatively insufficient for actual needs.

A similar occurrence is occasionally observed in the *blood* changes during pregnancy. An increase in juvenile types of erythrocytes and marked polymorphism (Zanfragoni, Soli, Varaldo and others quoted by Huessy), morphologic changes in the bone marrow, an increase in the size of the spleen (Berger), and other findings clearly express hyperactivity on the part of the entire hematopoietic system. A fall in hemoglobin, often noticed in early pregnancy, later as a rule disappears. At term the total blood volume is increased approximately by 15 per cent (Gueissaz and Wanner[64]), amounting to between 300 and 450 grams (Kaboth[65]). But during pregnancy hemolysis continues to a certain extent (pigmentation, iron needs of the fetus). A pathologic degree of red cell destruction, at times observed, has been ascribed more generally to toxic factors (Aubertin,[109] Oettingen,[66] Schneider[67]), or more specifically to an exaggerated hemolysis (Rowland[68]) due to insufficient development of antihemolytic bodies in the blood (Hofbauer[69]) or deficient cholesterol concentration (Benda[70]). Thus in some pregnant women a condition develops which resembles a pernicious anemia though it is not identical with this disease.

These few examples, to which others easily could be added, will suffice to demonstrate that certain biologic changes, observable during the premenstrual state, persist during pregnancy in a form which expresses their more or less perfect adjustment to definite fetal requirements.

Other adaptive changes are necessitated in the course of pregnancy by the passage of various substances from mother to fetus. In the main they consist in end-products of fetal metabolism thus imposing upon the mother the duty of their elimination or chemic destruction. The entrance of such chemically active substances, which act on the mother in some form of stimulation, now is an established fact. Only in this manner can be explained observations made, e.g., on the pyopagic Blazek sisters (Schauta) or in many experiments with artificial parabiosis by joining two female animals and controlling the effect of impregnation of the one on the other. The nonpregnant animal develops in genitalia and breasts as well as in hypophysis, adrenals or thyroid all those structural changes which are characteristic for pregnancy (Matsuyama,[71] Nissen,[72] Schmidt[73]). The assumption that an important rôle is played in the physiology and pathology of pregnancy by placental ferments (Hofbauer[69]) is based on strong evidence. The entrance of fetal hormons into the maternal organism cannot be any longer doubted since by newer tests it now is possible to ascertain the male sex of the fetus in utero by the presence of testicular hormonic substances in the maternal blood (Luettge and Mertz,[74] Sellheim,[75] Streck[114]).

Introduction of such substances, outside of carbon dioxide and

other waste products of fetal metabolism, necessarily will cause reactive changes in the mother. Many writers insist of late that, e.g., blood changes in pregnant women do not express a merely negative defense reaction but represent a definitely positive factor, that they manifest the accomplished adaptation to profound biochemic alterations and indicate the reestablishment of a temporarily disturbed equilibrium (Abderhalden, Guggenheimer, Sellheim[76]). This might be so, but unfortunately neither the older nor this newer definition and interpretation of such changes brings us nearer to the solution of that one most important problem in the physiology of pregnancy: Which one of these many biologic changes is due to the influence of this or that substance known to pass from fetus to mother? It seems obvious that we shall not be able to make any claim to a satisfactory understanding of the physiology of pregnancy as long as the answer to this particular question has not been supplied.

Therefore, we can only surmise in a general way that certain other biologic changes during pregnancy, not so far mentioned here, represent reactions or adaptation to stimuli coming from fetus or placenta.

There is a physiologic increase of the fibrinogen contents (Dienst, Kroesing,[78] Mueller,[77] Oettingen,[79] Wesselow and Wyatt[25]) and of the cholesterol concentration of the blood (Albrecht and Weltmann, Aschoff and Buemaster, Kuerten,[80] Neumann and Herrmann[81]). Either of these conditions has been thought to explain another characteristic phenomenon of pregnancy, namely an increased speed of erythrocyte sedimentation, confirmed by all investigators (Baer and Reis,[82] Linzemeier,[83] Woehlisch and Bohnen[84]). That these same changes, probably in some way connected with altered liver function, are also noticed in inflammatory processes is not surprising because they actually express only greatly accelerated metabolism which prevails in pregnancy as well as in inflammations. These last mentioned blood changes can serve as a good example of the direct association and mutual dependence on each other of a number of biochemic changes typically observed in pregnancy.

In a similar manner we can trace another series of phenomena, commonly noticed in pregnant women, as caused by the anomalous behavior of the vasomotor system which in turn is so closely related to changes of endocrine function and of the physicochemic condition of the blood (Seitz,[20] Zondek[63]). Angiospastic states in capillaries interfere with the flow of the blood through them, and secondarily this fact plays an important rôle in the known instability of the blood pressure and probably also in histologic-anatomic changes of parenchymatous organs (Hinselmann[85]).

If we, with Aschner, define the term "constitution" as implying

not alone the total of hereditary endowment of an individual (Mathes) but as including as well all the changes later brought about by external influences, we can state that pregnancy causes in woman a profound constitutional change. Since the pregnancy reactions in general imply an increase of the functional ability of the various organs, they are as a whole advantageous. Since many of these changes are permanent, the woman starts at her second pregnancy in a certain sense as another, biologically better equipped, individual, a fact fully supported by clinical experience.

FUNCTIONAL CHANGES CAUSED BY ALTERED TOPICAL RELATIONS OF ABDOMINAL ORGANS

Elevation of the diaphragm and interference with its respiratory movements late in pregnancy does not in itself impede gas exchange. Changes in the configuration of the thorax preserve the normal vital capacity of the lungs, of course, granted that the woman's thorax is not distorted by a congenital or acquired deformity.

Through elevation of the diaphragm the heart becomes dislocated, the apex finally being pushed two cm. to the left. The degree of this torsion is determined by the type both of the thorax and of the heart. In the type of heart, which is described by J. Bauer as arthritic, the displacement leads to a practically horizontal position of the heart. This turning causes a twisting particularly of the pulmonaris and this accounts for the physiologic systolic murmur commonly heard in the left second interspace, especially with patient sitting or standing up, when the dislocated heart also is pressed against the sternum.

Enlargement both of the total volume of blood and the area of its distribution calls during pregnancy for augmented work on the part of the heart. The mass of the heart becomes heavier, but since this increase, as pointed out by Jaschke, is only proportionate to the increase in body weight, it cannot be properly termed an hypertrophy. Electrocardiographic studies also seem to exclude an actual hypertrophy but indicate enlarged function by the fact that all the waves of all the leads in all postures are of a greater amplitude (Smith[86]). The heart takes care of the extra load by a faster rate of contractions, and by increase of the blood volume expelled with each contraction or within a minute (Frey,[87] Weiss[6]). It might be emphasized in this connection that recent studies on dogs have shown increase of cardiac output not only during pregnancy but also, though to slighter degree, during the estrus cycle (Stander, Duncan and Sisser[88]). Even hearts frankly diseased will often bear up remarkably well, since the ability for adequate adaptation to increased needs is solely dependent on the condition of the myocardium (Herrick,[89]

MacKenzie,[90] Prassulides[91]). The break in compensation during pregnancy, as a rule, is brought about by extracardiac factors, most often by renal complications or infections. Overstrain in athletically inclined women during pregnancy may produce a relative cardiac insufficiency closely bordering on the pathologic (Daly and Strouse[92]).

Venectasies are the result of mechanical factors combined with a constitutional deficiency. Pressure exerted by the pregnant uterus interferes with the return flow of the blood to such an extent that by a change from the horizontal to the vertical posture the amount of blood contained in the lower half of the body is almost doubled (Fick[93]). While in nongravid women the venous pressure in arms and legs is the same, even early in pregnancy the venous pressure in the lower extremities always is found higher than that in the ulnar veins (Runge[94]). The formation of venectasies through interference with the blood flow is directly dependent upon anomalies of the elastic tissue noticeable all through the body (Fischer[95]).

Pressure of the pregnant uterus against the ureter certainly plays only a minor rôle in the origin of the so-called pyelitis of pregnancy. Easy and effective drainage of the kidney in many instances is prevented by fairly common congenital ureteral strictures or due to kinks resulting from redundancy and folding of otherwise normal ureters (Eisendrath[96]). Varying degrees of dilatation in the upper urinary tract occur in up to 80 per cent of normal pregnant women (Jolly, Kretschmer and Heaney,[97] Strassmann[98]). This dilatation very likely often is not caused by any stricture or compression, but like atonic constipation in pregnant women is only the expression of disturbed function of the sympathetic nervous system (Stoeckel[99]). Pediatricians have found pyelitis to be a common disease of early childhood, and also among children the right ureter is the one most often affected. Pregnancy itself perhaps only very rarely represents the actual cause for a pyelitis but frequently acts as a predisposing factor, merely lightening up a preexisting condition (Kermauner,[100] Stoeckel,[99] Williams[101]). This view is strongly supported by the fact that a pyelitis often is observed to continue long after delivery, i.e., long after the assumed harmful compression of the ureter certainly has ceased (Rosinsky[102]).

OTHER ADAPTIVE CHANGES

Adaptation to the needs of the growing fetus is accomplished not solely by morphologic, chemic or functional changes of the mother.

The fetus is not a parasite in the common meaning of this term. He abstracts automatically from the maternal blood all the material he requires, and occasionally even to a degree not any longer compatible with the mother's health, but at the same time he always

acts also as a forceful stimulus on the mother. Under normal conditions during pregnancy her desire for food increases markedly. In a recent meeting of physiologists in Vienna (1925) the obvious difference between hunger and appetite was thoroughly discussed. It seems that while hunger like thirst in general simply implies the existing need for the intake of nourishment, appetite more specifically expresses the desire for special food substances. It is reasonable to expect that a careful analysis of the so-called longings of the pregnant woman will throw additional light on this particular problem of appetite. Frequently such longings precisely express a specific need of fetus or mother. In the light of facts mentioned in foregoing pages we might appreciate the rationality of the occasional craving for chalk, for sweets, acids or alkalis. In regard to the very common craving for acids I might emphasize that, in contrast to prevailing opinion, in the overwhelming majority of cases during pregnancy the gastric secretions show a state of subnormal acidity while hyper chlorhydria actually is rare (Kehrer,[4] Krahmer-Petersen[103]). Of course, this does not preclude the possibility that at times such longings are truly perverted, or that the intake of specific food material is insufficient as the result of external conditions or of ignorance. There still remains a field for intelligent food supervision in prenatal care.

Adaptation to fetal needs, however, is accomplished not only by greater food intake but also by its better metabolization and by restriction of its utilization for the mother herself. This latter factor more recently has been studied by Russian physiologists (Reprieff[104]) Some of the chemical changes in body fluids indicate better metabolization. The common desire of gravid women for inactivity, their longing for rest and sleep may be but the expression of an automatic restriction in the utilization of food for their personal needs.

PATHOLOGIC PHYSIOLOGY OF PREGNANCY

While admittedly lying within the boundaries of physiologic normalcy some of these structural, chemical and functional changes incident to pregnancy, as already pointed out, often are accompanied by clinical manifestations which in the nonpregnant individual always —and even in the pregnant woman at times—are indicative of a truly pathologic condition.

Not directly concerned in this paper with the relation of pregnancy to the origin of disease, I shall consider here only those symptoms in the pathophysiology of gestation which merely suggest disease. Many recent investigators have endeavored to establish the etiology of such pathologic states and to discover the specific cause for each of them. In view of our undeniable ignorance concerning

the specific physiologic reaction to a specific stimulus in normal pregnancy it seems surprising that most investigators make it their task to reveal the nature and degree of abnormal reactions both to normal physiologic and clearly pathologic stimuli, and that they have selected as the favorite field for their researches the so-called toxemias of pregnancy.

That laborious studies along these lines so far have failed to yield conclusive results, in my opinion, is due to several causes. First of all, too exclusively the growing ovum has been looked upon as the only possible source of all the changes observed in a pregnant woman. Our present knowledge that a large group of phenomena of pregnancy, including the presence of toxic substances and of proteolytic ferments in the blood, can also be observed during the premenstrual state, clearly forces us to include dysfunction of the ovaries as a possible other direct or indirect cause of disturbances which manifest themselves early in pregnancy, as is the rule with the so-called toxemias. And secondly, there actually does not exist agreement concerning the very term "toxemia." To those authorities who at present differentiate specific types of toxicoses, we find strenuously opposed others who with equal justification regard toxemia as a sort of entity which expresses itself under a variety of clinical pictures. The term toxemia seemingly has arisen from the wide distribution of the various lesions found in these cases and from the fact that concurrent structural changes are of a degenerative rather than of an inflammatory character (Wesselow and Wyatt[25]).

In this problem, in my opinion, not sufficient consideration is accorded to still another characteristic common to so-called toxemias. Their clinical manifestations disappear either during pregnancy or soon after its termination. Often it is this characteristic alone that enables us to recognize in the individual case a pathologic state as a toxicosis, and to differentiate it from a truly pathologic condition which also may manifest itself first during pregnancy but will persist after the expulsion of the fetus. A supposedly harmless toxic nephropathy of pregnancy in a considerable percentage of cases reveals itself a year or more later as a true nephritis (Baisch, Harris,[105] Zangemeister, Zondek and Jakobovitz[106]).

We might then with more justification state that pathologic-physiologic manifestations during pregnancy, and especially those commonly but incorrectly ascribed to a toxic state of the blood, primarily express only the inability of the maternal organism to adjust itself promptly or completely to the various exigencies imposed on it by pregnancy. Very often this deficiency of perfect adaptation is caused by a failure on the part of but one organ or organ system, and in this

manner we can plausibly account for the variety of clinical pictures. Organs prematurely arrested in their postfetal development or slightly damaged by preceding disease may be unable to augment their function to the required degree, especially during the first pregnancy. As the result of further structural change incident to pregnancy they may completely break down in function.

Inadequate response to needs must not by any means give rise to the accumulation of toxic substances in the blood. The pituitary gland is an important member of the endocrine system. With changed ovarian function during pregnancy it undergoes marked and well-known morphologic and functional changes. The pituitary exerts its influence on such widely differing processes as tissue growth, carbohydrate metabolism or water distribution in the body. An incongruous reaction of this gland during pregnancy then might play a part in the causation of such pathologic signs as swelling of the face or hands, of glycosuria or the formation of edema, phenomena which under these conditions certainly would not be due to a toxemic state.

Recent investigators seem to have established a direct connection between the general habitus of the woman or her nervous-emotional make-up to some of the presumably toxemic disturbances of pregnancy. H. Strauss[97] speaks of a special disposition to albuminuria existing in women of an asthenic habitus. Draper[107] ascertains that larger, heavier built women of masculine type, who in general display the insignia of previously increased pituitary function, are prone to develop under the stimulus of pregnancy hypertension or nephritis, a fact which suggests that idiopathic hypertension and nephritis possibly are but different expressions of the same disease. Various writers assert that the severe type of hyperemesis is met only in highly emotional women. Chemical studies, especially of early cases of hyperemesis, manifest the signs rather of inanition than of a toxemia. This inanition is primarily caused by idiopathic and psychogenic factors leading to anorexia, nausea and actual vomiting (Frey[108]).

It will be superfluous to quote examples or cite authorities for the assertion that a previously damaged organ may during pregnancy be further or permanently impaired as the result of added structural changes or under the strain of greatly increased function.

Evidences of inadequate adaptation in form of pathologic clinical symptoms are common within the first trimester. They might persist up to the termination of gestation, but the usually early restoration of the disturbed equilibrium, chiefly through the influence of that superimposed mechanism which controls harmonious organ interaction, is one of the outstanding characteristics of the normal and pathologic physiology of pregnancy.

CONCLUSIONS

During the week preceding the menstrual flow ovarian hormons initiate profound biologic changes not only in the genitalia but throughout the organism, which definitely manifest the consistent and propitious preparation of woman for impregnation. They necessarily are in evidence at the moment of the implantation of a fertilized ovum. It, therefore, is unjustifiable to explain any of these biologic changes as due to some foreign protein, cytolysin or any other factor dependent upon the implantation process. They are due alone to ovarian hormons.

Changes, primarily the result of cyclic ovarian function, during pregnancy are modified, and others added as gestation progresses.

The widespread and varying morphologic, chemical and functional alterations, which characterize the normal physiology of pregnancy, express the gradual adaptation to exigencies created by pregnancy. These requirements consist chiefly in qualitative and quantitative needs of the fetus for building materials and energy, and for adequate disposal of end-products of fetal metabolism and of other chemically active substances passing from fetus to mother. Later in pregnancy adjustment is required to certain topic derangements within the abdominal cavity caused by the enlarging fetus and uterine tumor.

In the constitutionally normal and healthy woman this necessary adaptation will be fully achieved. She will continue during pregnancy in a state of health.

In the woman who is constitutionally deficient, or in whom certain organs or organ systems through premature arrest of postfetal development or through preceding disease have become unable to respond with an increase of function to an increase of demands, adjustment is likely to be accomplished only slowly or imperfectly. Inadequate adjustment manifests itself in symptoms and clinical findings which in the nonpregnant individual always indicate a truly pathologic condition. They constitute the pathologic-physiology of pregnancy, best and most often expressed in clinical pictures commonly described as the toxemias of pregnancy.

Additional structural changes during pregnancy and the strain of greatly increased functional activity may impair an already injured organ to such an extent that complete restitution later becomes impossible. This transition of pathologic-physiologic changes into actually pathologic conditions, this transgression over the always indistinct borderline between merely temporary disturbance and true disease, as a rule is gradual. Often the fact that this change actually has occurred cannot be established until some time after pregnancy has ended.

Pregnant women, better and more conveniently than sick individ-

uals or animals in laboratory experiments, offer most favorable opportunities for following step by step the development of structural and functional derangements in all the larger parenchymatous organs and especially the endocrine glands, and for observing in their incipience certain disturbances of general or special metabolisms. A clearer understanding of the specific stimuli and conditions which during pregnancy lead to all these marked alterations could not fail to enlighten us also concerning the primary causes of various diseases or concerning those specific conditions under which slight impairment of one kind or another is likely to develop into actual disease.

The assumption seems justified that, with further addition to our knowledge concerning the general biologic effect of cyclic ovarian activity, a careful analysis of the premenstrual reactions of the individual woman might enable us to predict with some certainty how, at some later date, she is likely to adjust herself to the demands made by a pregnancy.

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Metropolitan Building. (*For discussion see page* 126.)

STERILITY ASSOCIATED WITH HABITUAL AMENORRHEA RELIEVED BY X-RAY THERAPY*

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I

AMENORRHEA associated with sterility is not uncommon. I have encountered it 74 times in a series of 1,450 consecutive cases of sterility. As a rule it renders the prognosis less favorable. Any measure which restores the menstrual function necessarily improves the prognosis, for the cause of the menstrual abnormality, other things being accounted for, may also be responsible for the sterility.

Cases of spontaneous cure are occasionally encountered, and pregnancy occurs when it is least expected. Three out of a total of 54 cases of sterility associated with amenorrhea and oligomenorrhea came under my personal observation between December 4, 1923, and December 31, 1925. They serve as a basis of comparison with the incidence of pregnancy occurring during this same period of time in twelve similar cases that were subjected to mild x-ray treatment. When pregnancy occurs spontaneously in these cases, the patient may regard herself in one of the phases of amenorrhea to which she has become habituated, and subjective symptoms such as nausea or vomiting may not lead her to suspect the true condition. In such cases the last ovulation following the last menstruation contributes the ovum which has become successfully fertilized.

The sterile patient complaining of amenorrhea must necessarily be less susceptible to conception than one whose menses are in all respects regular. For example, a woman who has a menstrual period

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twice a year has only one-sixth the normal number of ova available for impregnation. The presence or absence of the menstrual phenomenon is from all the evidence so far obtained, and until some other reliable method be developed, a fair indication of the functional activity of the ovaries. It is obvious that by increasing the number of a patient's menstrual periods, or better, the corresponding number of ovulations, that we shall improve proportionately her chances for impregnation.

Many measures have been tried from time to time to regulate the menses with varying results, too often based upon empirical grounds rather than upon scientific evidence. The most successful, perhaps, have been the gland extracts. The happy results, sometimes brilliant, in the experience of many have, however, been incapable of repetition in the same hands or in those of others. For this failure to get uniform results in the treatment of sterility associated with amenorrhea, our lack of knowledge of the relationship between cause and effect has been chiefly responsible. Another important reason is the fact that gland extracts have been prèpared according to different methods and vary widely, with the exception of thyroid and adrenalin, in their chemical structure and pharmacologic action.

Through the therapeutic use of the x-ray in the treatment of female genital bleeding a better understanding of one phase at least, of the relationship between ovarian function and uterine function has been reached. When uterine bleeding due to fibromyomata was treated by fractional x-ray doses, it was common experience to find that the first or second menstrual period would be increased and that a cumulative result was obtained after several treatments with the x-ray, the bleeding gradually diminishing and finally ceasing altogether. The effect of the x-ray is, as is well known, principally upon the ovaries and secondarily upon the uterus. We may, therefore, assume that mild doses induce certain changes in the ovaries which are expressed by increased uterine bleeding, while severe doses of the x-ray manifest themselves eventually by the disappearance of uterine bleeding. Apparently there is a quantitative as well as a qualitative relationship between x-ray dosage on the one hand and changes in ovarian structure and function on the other.

I shall not enter into the theoretical discussion of the so-called "stimulating" effects of the x-ray in contradistinction to the term "irritation," as we understand it in pathology. The biologic evidence is too scant to enable us to speak with precision on this point. Whether or not every application of deep rays first induces a certain degree of cell destruction or whether it simply stimulates the cells or organs, or the whole organism to increased function or growth, it is impossible as yet to determine. Certain secondary effects of ir-

radiation appear to be specific, as, for example, the increase in the coagulability of the blood and the formation of connective tissue observed so commonly in carcinoma therapy. It is difficult, nevertheless, to be certain that there may not have been a primary cell destruction to which these effects were secondary.

Geller's experimental work dealing with the question of the stimulating effects of the x-ray is suggestive but not yet conclusive. He found that irradiation of the ovaries of rabbits and rats with 5 per cent of the human skin erythema dose was followed by no ascertainable histologic effects in the excised ovaries. Ten per cent of the skin erythema dose, however, induced a definite diminution in the primary follicles which also showed degenerative changes. He therefore concluded that the *histologic changes passed at once from inaction to destruction.* When 20 per cent or 30 per cent were used the destructive effects upon the ovary were noticeable in the first weeks following the irradiation. A great many ripening follicles were still present but most of them showed signs of degeneration. These results incidentally contradict the accepted notion that the x-ray exerts a different influence on the different types of follicles, because the primary follicles and the larger follicles are equally affected. Whether or not these results obtained in the rabbits and rats can be assumed for the human is naturally problematic.

Inasmuch as amenorrhea was generally held to be due to an underfunction of the ovaries, Van der Velde began in 1915 to treat amenorrhea and oligomenorrhea by irradiation of the ovaries. His work was followed chiefly by Flatau and Thaler who used small doses of the x-ray in the treatment of amenorrhea. Flatau irradiated with a single x-ray dose equivalent to ⅓ of the castration dose. He treated 38 cases and found that in 25, the menstruation set in normally in the course of three to six weeks. In 12 more cases by treating only one field with a larger focal distance (30 cm. instead of 23 cm.) from the back, in order to embrace and affect surrounding tissues, vessels and nerves in the irradiation zone, 10 were cured; four cases out of his series became pregnant.

A still larger series of cases is reported by Thaler who treated all sorts of menstrual disturbances by weak doses of the x-ray. He uses milder doses than Flatau. One hundred forty-seven cases were irradiated by him. Of 62 cases of primary and secondary amenorrhea, 40 were cured. In 32 cases with too frequent menstruation due to an underfunction of the ovaries, 11 resulted in the return of regular periods. Out of 18 cases with abnormally long intervals and abnormally weak periods, 12 resulted satisfactorily. *Five women out of 80 with amenorrhea and oligomenorrhea became pregnant* in the first month following the treatment.

These results according to Martius[1] have been confirmed by Recasens, L. Seitz, Mansfeld, C. Schonhof, Meiner, Groedel and others. Wieloch appears to be the only one who feels that the treatment is a very uncertain one. A. J. Rongy[2] reports 13 cases treated by I. S. Hirsch with "stimulating" doses of x-ray, in five of whom the menstrual function was reestablished.

Mansfeld reported three cases of pregnancy following x-ray treatment of hypomenorrhea; Meiner and Aaron, one case; Caufman, one case, and Kraul, one case. Linzenmeyer and Thaler have reported pregnancies following weak irradiation of the ovaries in cases with increased menstrual periods (polymenorrhea).

THEORIES OF MANNER IN WHICH THE X-RAYS INFLUENCE THE OVARIES AND RESTORE THE MENSES IN AMENORRHEIC CASES

Flatau thought that the x-ray exercises a simple functional irritation upon the underfunctioning ovaries. Thaler, however, felt that the process was more complicated and that the corpus luteum which often persists in cases of amenorrhea undergoes a regressive change through the action of the x-ray. He further advanced the theory that the nonspecific protein bodies which result from the breaking down of the irradiated areas may also be responsible for the changes in the menstrual periodicity. This notion has since found support in the analogous results induced by protein bodies and the x-ray upon the metabolism of water, mineral and the hydrogen-ion concentration of the blood as found by Chr. Kroetz of Greifswald and later Anderson of Kiel.

The secondary effect of weak x-ray doses upon the fetus was studied by Martius and Franken. Six white mice of different strains were subjected to weak doses of the x-ray. The animals were selected after determining their mating and litter-dropping capacity. Eight days later five female mice were mated with five males of a foreign blood strain. All of these with the exception of one pair bore young after 21 to 25 days. The given dose was not sufficient to cause temporary sterilization. The number of young, however, was strikingly diminished for each pair. Whereas formerly they bore four to nine young, the number was now two to four, in other words a reduction of fertility to less than one-half. The mortality of the offspring was extraordinarily high. They also exhibited retarded growth; their skin was coarse and the hair on the head, as well as on the back, especially between the shoulder blades, was thin and scrubby. The animals looked thin and miserable and after six months weighed 16-18 grams instead of 23-25 grams. Younger animals similarly treated failed to become pregnant after six months. Martius concluded that there is always a certain amount of destruction of germinal substance

induced by "irritation" x-ray therapy. But these effects produced by animal experiments do not hold for the human being. So far not a single instance of a malformed fetus has been reported following x-ray treatment for myopathic conditions. Because of Geller's experimental results and his own work, Martius recommends careful x-ray dosage in the obstinate cases of amenorrhea as a last resort only. In cases of oligomenorrhea, as well as polymenorrhea, he feels that instead of a normal return of the menses there may ensue an actual permanent termination (premature climacterium). Seven out of thirty-two women in Thaler's series who were irradiated for polymenorrhea became amenorrheic.

H. B. Mathews[3] investigated the effects of radium rays upon ovarian tissue. He found that after exposure of the ovaries to from 600 to 800 mg. hr. pregnancy can and does occur, but doses above these figures cause sterility. Young healthy ovaries would stand much larger doses of radiation than older and less active ones.

The effect upon a fetus in utero by the irradiation is, however, different. Harold Bailey[4] concludes from his study of the literature and his own personal experience that in the treatment of menorrhagia in the childbearing period complete sterility is preferable to the possibility of a damaged germ plasm. He questions whether radium or x-ray irradiation should be used to destroy the ripe follicles, leaving the immature ones injured but capable of development. He makes this statement entirely upon the strength of the experimental work on lower animals but does not feel justified in considering any of the available clinical records as adding conclusive evidence in this regard. His further conclusion is that irradiation of the ovum during early gravidity should never be permitted. "Radiation in late pregnancy while it may not produce gross abnormalities at birth may hinder the growth and development of the child in later life."

So constant is the lethal result upon the young embryo that abortion or premature labor is very common, and this fact has been utilized in the induction of abortion in certain cases of pulmonary tuberculosis complicated by pregnancy. Where the pregnancy goes on to term the child exhibits abnormality in more than 90 per cent of the cases; so certainly that Seitz regards it a matter of urgent necessity to induce abortion in every case where abortion does not set in spontaneously in cases subjected to castration or carcinoma dose of the x-ray.

From Mathew's questionnaire including 874 cases of radiated women in childbearing age collected from all parts of the United States, 39 pregnancies occurred. From these 39 pregnancies 20 full-term normal babies were delivered. There were 15 abortions or miscarriages and three premature labors, making the ratio of abortions to normal labors 1 to 2.6, whereas in Germany the ratio is as 1 to 2.3

in 1,512 cases. The estimated ratio of abortions to normal pregnancies in the United States is as 1 to 3 or 4, whereas in Germany it is as 1 to 5 or 6. Only one patient in my series out of nine who became pregnant aborted. This patient aborted twice in succession.

If x-ray therapy is to be adopted in the treatment of sterility associated with amenorrhea it becomes a matter of great importance to determine what type of cases may be benefited and what type of cases may perhaps suffer still further loss of function. Martius summarized his conclusions on this point as follows:

1. The ovarian insufficiency may be due to a primary numerical deficiency in functioning follicles. In this case mild doses of the x-ray may do no good. They may even cause damage.

2. In a milder degree of ovarian insufficiency the amenorrhea or oligomenorrhea may be due to the fact that the follicles do not mature properly. Consequently there is no corpus luteum formation. Because of the absence of the inhibitory control of the corpus luteum the follicles ripen in excess and never or very seldom reach full maturity. As a result of this excessive immature ripening and cystic atresia of follicles the ovary becomes the seat of the so-called small cystic degeneration. Should mild doses of the x-ray be used then these immature follicles designated by Borak as "inadequate" become destroyed and in their place properly maturing follicles which may develop to the point of corpus luteum formation can ripen every four weeks and thus give rise to regular menstruation.

R. Schroeder advances the theory that the premature death of the ovum induces a premature regression of the corpus luteum. With the inhibitory control of the latter lacking, follicles may begin to ripen excessively and induce polymenorrhea. Through the action of the x-ray which affects all sorts of follicles, the intervals between full maturation of individual follicles may become greater, and amenorrhea results even without the intervention of a corpus luteum. There is thus a definite loss in parenchymal ovular structures, a result which can also be obtained, as first reported by Pape, when only one ovary is irradiated.

The dosage of x-ray now generally employed is practically the same as that recommended by Borak and is as follows:

For amenorrhea, 5-10 per cent of the skin erythema dose.

For oligomenorrhea, 10-15 per cent of the skin erythema dose.

In cases of bleeding, when it is desirable to reduce the flow, 15-35 per cent of the skin erythema dose is given.

When it is desirable to sterilize the patient, 25-50 per cent of the skin erythema dose is given.

A great deal depends upon the age of the patient, the apparatus used and the dosage necessary to produce a skin erythema. Martius believes with Borak in the preferable one-sided castration in cases of metrorrhagia in women younger than forty instead of bilateral irradiation.

II.

The present report deals with 12 cases of sterility associated with amenorrhea or oliogomenorrhea of milder and severer degree; nine of these patients have become pregnant following the use of mild

doses of the x-ray, the remaining three have so far not become pregnant. In the light of animal experimentation and reported clinical cases in medical literature, they should prove of some value.

CASE 1.—H. S., thirty-two years old, married twice; first marriage was fourteen years before, the second marriage was six years before. Menses began at thirteen years of age, always irregular every three to four to six months. Her last menstrual period was December, 1922. Uterine insufflation was done March 16, 1923, and her tubes proved to be patent. Both adnexa were enlarged and prolapsed, the left larger than the right. March 16, 1923, she was given thyroid extract and ovarian residue. April 5, 1923, the same things were prescribed. These failed to bring on the periods. December 5, 1923, 1/10 skin erythema dose (Dr. Charles Gottlieb). December 16, 1923, again 1/10 skin erythema dose. After an amenorrhea of twelve months she started to menstruate December 20 lasting to the 30th, very profusely and passed one clot. On examination the adnexa were found to be definitely reduced in size. There were no periods between December, 1923, and March, 1924, when she was examined and the uterus was found to be enlarged to the size of a two months' gravidity. Quickening was felt May 12, 1924. October 7, 1924, cesarean delivery at the Woman's Hospital of a boy weighing seven and a half pounds. One menstrual period postpartum, April 6 to 10, and, when last seen on January 18, 1926, there had been an amenorrhea for eight months, when examination showed that she was not pregnant.

CASE 2.—M. K., thirty years old, married eight years. Menses began at fifteen years, always irregular every three, four, six or twelve months, of six days' duration, and profuse. Her last menstrual period was December 1 to 5, 1923, and on examination both ovaries were found to be distinctly enlarged and one and a half times the normal size, prolapsed, and hard but not tender. January 15, 1924, uterine insufflation was done and her tubes were found patent. March 22, 1924, x-ray stimulation (Dr. Charles Gottlieb), thirty-two ma. minutes, 200,000 volts to the right ovary (8 x 4) and on May 27, 1924, thirty ma. minutes, 220,000 volts to sella turcica. Her next period was August 1 to 6, 1924. She flowed moderately the second and third days and scantily for three days; another menstrual period September 12 to 18, 1924. September 19, 1924, another uterine insufflation and tubes were found patent. The next period was October 18 to 24, 1924. March 21, 1925, the patient reported that there had been no bleeding since October and the uterus was found to be gravid two months. Quickening was felt July 1, 1925, and November 18, 1925, she was delivered of a male child weighing eight pounds and one and a quarter ounces. In this case no opotherapy was used.

CASE 3.—L. C., twenty-four years of age, married three years. Menses began at age of thirteen, very irregular, every three or four months; at the age of eighteen she had a period of amenorrhea lasting eight months. Her last menstrual period was July 4, 1923. On examination January 23, 1924, both adnexa were found to be prolapsed and there was a definite cystic enlargement of the ovaries. January 30, 1924, she was given thyroid and ovarian residue. February 26, 1924, uterine insufflation was done, and the tubes were found patent. She stained February 28 until March 2 following the insufflation. March 6, 1924, x-ray stimulation after an amenorrhea of eight months, by Dr. Charles Gottlieb, and again on April 4, 1924, twenty-eight ma. minutes, 220,000 volts to the region of sella on each side. The period after the x-ray treatment was July 6 to 13 and again July 28 to August 1, 1924. September 24, 1924, the uterus was found to be enlarged to the size of a six weeks' gravidity and there was no bleeding since August 1. She stained October

6 after a fright. December 21, 1924, she felt quickening, and on December 28, 1924, an approximately five months' female fetus which was perfectly formed, was aborted. May 28, 1925, she reported her last period was February 22 to 25 and four weeks later she stained for four days and then two weeks later again stained. First week of April she stained for three days. July 23, 1925, she reported her last period as May 12 to 18, 1925. August 20, 1925, the uterus was found to be definitely enlarged to the size of a two months' gravidity. Quickening was felt October 16, 1925. December 3, 1925, a six months' male fetus, which was perfectly formed, was aborted.

CASE 4.—A. S., nineteen years of age, married one year. Menses began at seventeen years, duration six to seven days. She had two periods in two years. February 2, 1922, on examination the uterus was found to be small, the adnexa not palpable. Her last period was five months before. She was given thyroid and lutein. February 23, 1922, she was given pituitary and ovarian residue, and her period started February 24 until March 4, after six months of amenorrhea. May 31, 1922, she was again given ovarian residue. From October 10 to 21, 1922, she received injections of pituitrin. Her next period started October 27 and lasted until November 4, 1922, after a period of amenorrhea of seven months' duration. She had another period November 26 for one day. December 19, 1922, uterine insufflation was done and her tubes were found patent. Her next period was December 20 to 27, 1922. March 3, 1923, she reported no period since December, 1922, and was given thyroid tablets. She stained March 10 to 12 scantily after a period of two weeks' amenorrhea. Her next period was April 26 until May 6, 1923, and was very profuse; another period July 28 to August 4, 1923. After five months' amenorrhea the next period was March 1 to 5. X-ray treatment by Dr. Charles Gottlieb April 11, 1924, thirty ma. minutes, 220,000 volts to the right ovary. May 16, 1924, fifteen ma. minutes, right ovary, 220,000 volts, and 30 ma. minutes, left ovary, 220,000 volts and the next period was June 1 to 7, normal; again July 10 to 16 and August 28 to September 3, 1924. November 10, 1924, she reported that she started to stain October 18 and on examination the uterus was found to be as large as six to seven weeks' gravidity. November 29, 1924, she was still bleeding and a light curettage was done. Her next period was February 24 to 28, 1925. May 7, 1925, the uterus was found to be as large as a three months' gravidity, and there had been no bleeding since the February period. Quickening was felt about June 10 to 15, 1925. November 30, 1925, birth of male weighing nine pounds and four and a half ounces.

CASE 5.—F. B., twenty-two years of age, married one year. Menses began at thirteen years, always irregular, every five to six to seven to ten to twelve weeks, lasting five to six days. February 4, 1925, she stated that her last period was January 24 to 29, 1925, fourteen weeks after her previous menses. On examination the right adnexa were found to be definitely thickened, and the left adnexa was palpable and slightly enlarged, tender and prolapsed. February 16, 1925, she was given anterior pituitary tablets. X-ray treatment by Dr. Ira Kaplan March 12, 1925, right and left anterior abdomen 25 per cent. Her next period was April 1 to 4 about eleven weeks after the last period in January. June 4, 1925, on examination the uterus was definitely enlarged to six weeks' gravidity. Quickening was felt August 25, 1925. Birth of female child weighing seven pounds and six and a half ounces on January 16, 1926.

CASE 6.—L. S., thirty-three years of age, married sixteen years. Menses began at seventeen years, always irregular, every three, six, nine or twelve months. Her last period was September 26 to October 1, 1924. In 1913, following a curettage for

profuse bleeding, she had an amenorrhea for twelve months. October 16, 1924, on examination the uterus was plump; the right ovary was considerably enlarged. October 17, 1924, the uterus was insufflated and the tubes were found patent. The following period was October 19 to 26, 1924, one week early. The following period was December 25, 1924, to January 4, 1925. X-ray treatment by Dr. Ira Kaplan January 12, 1925, right and left anterior abdomen 20 per cent; January 21, 1925, right and left posterior abdomen 30 per cent; January 30, right and left anterior 15 per cent and 10 per cent to thyroid. She began to bleed March 12 to 14. The period was profuse and painful. The next period was April 12 to 16 and again May 11 to 16, 1923. May 20, 1925, she was given anterior pituitary and thyroid tablets, and the next period appeared June 8 to 13, 1925. August 26, 1925, she reported no bleeding since June and her uterus was found to be two months gravid. Quickening was felt October 26, 1925. This patient was delivered March 19, 1926, of a male child weighing seven pounds and four ounces.

CASE 7.— M. W., aged twenty-nine years, married eight years. Menses began at fourteen years, irregular every three to four months, duration two to three to four days with moderate flow. On October 31, 1924, she reported her last period to have been August 20 to 25, 1924, which had been two months after previous one. On examination the right adnexa were found to be enlarged, firm, and somewhat tender. Uterine insufflation was done October 31, 1924, and the tubes found to be patent. The next period was January 5 to 10, 1925, and again February 12 to 15; these periods were painless. February 20, 1925, she was given anterior pituitary extract. X-ray treatment by Dr. Charles Gottlieb, May 20, 1925, and June 3, 1925, $\frac{1}{10}$ H. E. D. to each ovary, 200,000 volts. Without any intervening menstruation since February 12 to 15, when she was examined on July 27, 1925, the uterus was found to be enlarged to the size of an approximately ten to eleven weeks' gravidity. Quickening was first felt September 6, 1925, and she has advanced in pregnancy, the labor being expected February 15 to 28, 1926.*

CASE 8.—S. E., aged twenty-four years, married two and a half years. Menses always irregular every six to seven to twelve months. On July 21, 1924, she reported her last period as of October 4 to 12, 1923. X-ray treatment October 22, 1924, after an amenorrhea of practically thirteen months, to the right and left anterior abdomen 18 per cent; October 28, 1924, right and left posterior abdomen 18 per cent; November 11, 1924, right and left anterior abdomen 22 per cent, by Dr. Ira Kaplan. Her next period was December 9, 1924, and again January 11, 1925. Physician reported birth of a male baby October 15, 1925, weighing seven pounds and six ounces. No opotherapy was used.

CASE 9.—C. G., thirty-one years of age, married six years. Menses began at sixteen years, irregular every six to seven weeks. During past three years every three to four months and duration five to six days. On January 24, 1925, she reported that her last period was January 2 to 7 and on examination the right ovary was found to be exceedingly hard, spherical but not tender. February 3, 1925, uterine insufflation was done and her tubes were found to be patent. The next period was February 5 to 9; this was the first time in six years that her periods were so close together. X-ray treatment by Dr. Charles Gottlieb, February 19, 1925, $\frac{1}{10}$ H. E. D., 200,000 volts to each ovary. July 14, 1925, her physician reported that the patient was four months pregnant. No other data. No opotherapy was prescribed.

CASE 10.—M. R., thirty years old, married the first time thirteen years before for three years, second time ten years before. Menses began at fourteen years, always

*This patient was delivered of a male child weighing nine pounds and one-half ounce on February 26, 1926.

irregular every two to three months. Her last period was November 1 to 5, 1923, and on examination the cervix was found to be small, the right adnexa distinctly palpable, slightly enlarged and somewhat tender. The left adnexa were slightly palpable but not thickened or tender. The cervix was typically infantile on inspection. Uterine insufflation November 13, 1923; tubes found to be patent. Her next period was December 8 to 12, 1923. December 18, she was given thyroid and lutein. Her weight was 160 pounds. October 24, 1924, x-ray treatment by Dr. Ira Kaplan right and left anterior abdomen 10 per cent of the castration dose, and November 7, 1924, right anterior 45 per cent of the castration dose and left anterior 40 per cent of the castration dose. The periods were practically unaffected by the x-ray treatment except that the first menses following the treatment was a little more profuse and the next three menstrual periods more nearly of the four week type. After this the periods returned to the five week interval. The patient has not become pregnant thus far.

CASE 11.—J. M., twenty-eight years old, married three and a half years. Menses began at thirteen years; were always regular four week type of four to five days' duration. The last menstrual period was May, 1913, eleven and a half years before. On examination the uterus was found to be small, the vagina atrophic and the adnexa not palpable. Uterine insufflation showed the tubes to be patent. X-ray treatment October 30, 1924, to the right anterior abdomen 10 per cent; left anterior abdomen 13 per cent; November 6, 1924, right and left anterior abdomen 40 per cent; November 12, 1924, right and left posterior abdomen 15 per cent; and November 12, 1924, right and left pituitary 15 per cent. The patient reports no return of menses and no pregnancy.

CASE 12.—R. P., twenty-four years old, married two years. Menses began at sixteen years, always irregular, from a month to one year late. Her last menstrual period was July 20 to 25, 1923, one year before. On examination the vagina was tight, cervix exceedingly small to touch, the uterus apparently subnormal in size, right ovary palpable and somewhat enlarged, left adnexa not felt. Uterine insufflation was done July 29, 1924, and her tubes were found to be patent. January 21, 1925, x-ray treatment right and left anterior abdomen 25 per cent; March 17, 1925, right and left anterior abdomen 25 per cent and right and left pituitary 10 per cent; March 24, 1925, right and left posterior abdomen 20 per cent, and her next period was May 2 to 7, after an amenorrhea of 22 months. The next one was July 15 to 21, 1925. This patient has not become pregnant thus far.

SUMMARY AND ANALYSIS OF CASES

Inasmuch as these patients were treated for sterility and not only for the habitual amenorrhea, the other factors entering into each case had to be considered. The male factor being satisfactory in all, special attention was given to the question of patency of the tubes. These were normal in all the cases but two, in which tubal insufflation had not been done. A third factor was the possibility of endocrine deficiency. Therefore the gland extracts were administered in most of the cases. In view of the possible therapeutic influence which may be ascribed to these two measures, I have felt it necessary to analyze the cases carefully in order to determine the real value of the x-ray treatment in cases of sterility associated with amenorrhea.

a. When the first period appeared after *x-ray treatment* in the *pregnant group:*

Two weeks after treatment in one case
Three weeks after treatment in one case
Six weeks after treatment in one case
Seven weeks after treatment in one case
Two months after treatment in one case
Four months after treatment in one case
Five months after treatment in one case
No data in two cases

In the *nonpregnant group:*

Five weeks after the x-ray treatment in one case
Thirteen weeks after the x-ray treatment in one case after an amenorrhea of twenty-two months
No return of menses in one case

b. Opotherapy was given in the *pregnant group* as follows:

Preceding the x-ray treatment in five cases
After the x-ray treatment in one case
No opotherapy was given in three cases

Opotherapy was given in the *nonpregnant group* as follows:

Preceding the x-ray treatment in one case
No opotherapy was given in two cases

c. Uterine insufflation was done in the cases that became *pregnant* as follows:

Preceding the x-ray treatment in six cases
Preceding and following the x-ray stimulation in one case
No insufflation was done in two cases

In the *nonpregnant* group *uterine insufflation* was done:

Preceding the x-ray treatment in all three cases

Uterine insufflation preceded the x-ray treatment in pregnant group by:

Two weeks in two cases
Three months in one case
Five months in one case
Nine months in one case
One year and four months in one case
Two months preceding and four months after last x-ray treatment in one case

In the *nonpregnant group insufflation preceded x-ray treatment by:*

Six weeks in one case
Six months in the other cases

d. In four of the treated cases the hypophysis area was also irradiated; two of these patients were in the nonpregnant group. One of the pregnant group received irradiation to the thyroid as well as to the ovaries.

e. Six cases went to term thus far.

Of the patients personally delivered six gave birth to males and one to a female. The sex of the baby in one case is not recorded.

One patient had two miscarriages, the first a female at five months, the second a male at six months.

The average weight of the babies at term is seven pounds and 14½ ounces. The largest was nine pounds and four and a half ounces and the smallest was seven pounds and four ounces.

f. Of those who became pregnant:

Two were married one year
One was married one and a half years
One was married three years
One was married six years
Two were married eight years
One was married fourteen years
One was married fifteen years

Of those who did not become pregnant:

One was married two years
One was married three and a half years
One was married thirteen years

g. Conception took place following the x-ray treatment:

One month after x-ray treatment in two cases
Two months after x-ray treatment in one case
Three months after x-ray treatment in one case
Five months after x-ray treatment in one case
Six months after x-ray treatment in two cases
Ten months after x-ray treatment in one case
The same month in one case

As the duration of married life always enters into the consideration of the cause of sterility, it is well to note that of the nine patients who became pregnant, two were married only one year, one was married two and a half years and the remaining six were married three years or more. One of the latter dated her marriage fourteen years and another sixteen years. Inasmuch as the two young women who were married but one year suffered from marked amenorrhea, it may be justifiable to reckon the therapeutic value in favor of x-ray treatment.

Only in one of the successful cases was the finding noted that the adnexa were not palpable. In the eight others the ovaries were bilaterally or unilaterally definitely enlarged. This finding should serve as a guide, perhaps, in choosing the cases for therapy. It suggests the presence either of a persistent corpus luteum in some of the cases or it points to ovaries enlarged by excessive numbers of immaturely ripening follicles. The latter occurs in certain cases where polymenorrhea precedes the amenorrhea.

CONCLUSIONS

1. Habitual amenorrhea is associated with sterility in about 5 per cent of cases.

2. Pregnancy takes place in about 5.5 per cent of the untreated cases.

3. In nine out of twelve cases treated with mild doses of x-ray, pregnancy resulted (i.e., 75 per cent of the treated cases). Only one of these patients aborted. The rest carried to full term and gave

birth to normal children. Among seven of the latter personally delivered there were six males and one female.

4. X-ray irradiation of the ovaries resulted in restoration of the menses in eleven out of twelve cases of amenorrhea.

5. X-ray irradiation of the hypophysis area and the thyroid appears to have an adjuvant value. Two of the pregnant cases and two of the nonpregnant cases received hypophyseal irradiation. One of the pregnant cases also received thyroid irradiation.

6. Peruterine tubal insufflation and endocrine therapy are additional aids to the therapeutic action of the x-rays in cases of amenorrhea associated with sterility.

7. As the ovaries were found to be definitely enlarged before treatment in eight of the nine successful cases treated with x-rays, careful examination with regard to this point may prove of aid in selecting the cases of amenorrhea associated with sterility suitable for ovarian stimulation. When no ovarian enlargement is found, irradiation to the hypophyseal area or the thyroid, etc., may be more advisable and should certainly precede irradiation of the ovaries.

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(*For discussion see page* 130.)

THE CONSERVATIVE TREATMENT OF UNCOMPLICATED RETRODISPLACEMENT OF THE UTERUS*

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INTRODUCTION

IN CONSIDERING the problem embodied in the title of this paper, I have deviated somewhat from the path of custom and have included not only the treatment of uncomplicated displacement of the uterus, but certain other phases of the trouble as well. This unfortunately prolongs my introductory remarks, but is justified on the ground that they embrace certain features of the subject which I regard more important than the treatment of the condition itself.

In the brief span of ten years all departments of science have made phenomenal progress and it is obvious to all that the science of medicine has kept quite abreast of scientific progress in general.

Specialization has played a definite influential rôle in this evolutionary period, but specialization, while prominently displaying its burnished side of beneficence, at first, unfortunately, exposed a drab side of passionate radicalism. This feature of specialization has been largely overcome by repeated assaults, and, thanks to a sound philosophy, it has gradually been settling toward a rational conservatism.

The specialty devoted to the diseases peculiar to women has contributed a gratifying quota to specialization and, while there is still much to be desired from the conservative aspect, gynecology no longer can be regarded as ultraradical.

The conservative wave, starting as a faint ripple about twenty-five years ago, has developed into an expanding billow and the crest of the wave is not yet in sight. It is destined to broaden and ultimately will embrace certain pelvic disorders which are still looked upon as surgical.

We can scarcely accuse our eminent predecessors of ignorance with regard to the fundamental importance of conservative effort in dealing with organs, first, of fathomless systemic value and, second, in propagating the human family, yet the former practice of indiscriminate and ofttimes sacrificial surgery is wholly beyond the comprehension of men active in gynecology today.

Within the past decade certain genital disorders, heretofore regarded as wholly surgical, have fallen in the category of medical or at least semimedical conditions. These include the acute pelvic infec-

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tions, infected abortions, simple uterine displacements, uterine myomas and uterine carcinoma. To all of the conditions named operative therapy was formerly almost routinely applied.

During the past ten years progress along conservative lines has been almost beyond belief and it is quite safe to say that during this period operative gynecology has decreased at least 25 per cent.

It is probable, though I realize it is dangerous to deal in propheey, that the next ten years will see the conservative pendulum swing still farther, so much so that gynecology may not be the alluring surgical specialty it has been in the past. Indeed, it is quite conceivable that only a few pelvic conditions will be looked upon as truly surgical, such, for example, as pathologic displacements, partial or complete uterine prolapse, ovarian neoplasms, severe parturitional damage, frank pus collections and large pelvic neoplasms. It is not beyond hope that even some of these, especially uterine tumors, will rarely require surgery, since by early recognition and prompt irradiation they will not attain surgical proportions. Gross obstetric lesions will, I believe, be largely prevented by the adoption and practice of intelligent obstetric strategy and more skillful, as well as discriminating obstetric tactics.

Among the pelvic conditions which have presented a comely figure to the practicing gynecologist, a group which developed an early and abiding infatuation and one to which assiduous court has long been paid, was uterine displacements. Indeed, of the manifold disorders arising in the female pelvis, none have presented a more alluring physiognomy than malpositions of the womb.

Since the discussion of the title of my paper is governed by the qualifying term "uncomplicated," it seems proper that my interpretation of the phrase be explained.

There should be no serious difficulty, if difficulty at all, in defining and recognizing either a simple or a complicated uterine displacement.

Each type has characteristic features. I believe that most physicians would regard a retroposed uterus of relatively normal size, freely movable and occurring in young single women or young nulliparous married women as one of the uncomplicated variety. I am equally sure that most observers would also regard a uterus of normal size, one not constantly anterior or posterior arising in the type of patients to whom reference has just been made, as truly uncomplicated.

As regards the complicated or pathologic displacement, it is rarely found in young, single women or young women who have not borne children. The organ generally is in constant retroposition and in nearly all instances, owing to the hyperplastic alteration of its walls, it is frankly enlarged. The increased weight of the structure com-

bined with the intraabdominal pressure may imprison it in the hollow of the sacrum or it may thus be fixed as the result of periuterine infection. The condition usually is a sequel of parturition, so the displacement itself in most cases is associated with parturitional injury. A complicated displacement, then, is one associated with definite pathologic alteration in the uterus itself, in the circumjacent structures, or in both.

There is still another form of posterior displacement deserving mention. I refer to those cases so commonly found in highly neurotic, physically incompetent women.

The number of this variety operated upon is beyond computation. Have many, if any, ever been benefited? It is obvious that displaced uteri arising in patients of this so-called neurasthenic group are in no sense pathologic in themselves but rather a manifestation of the general passive or subnormal condition of the patient herself.

Symptoms.—Probably no conditions arising in the human body have been so falsely accused of creating symptoms, both systemic and local, as innocent, not pathologic, uterine displacements. For no other disturbances have such an array of therapeutic methods, both medical and surgical, been designed with almost equally uniform failure in affording symptomatic relief.

Normally, the uterine body is a freely movable organ and, so long as it is normal in size and freely movable, may it not be, from a physiologic as well as from an anatomic standpoint, as normal posteriorly as it is anteriorly?

The teaching that the uterus is maintained in position by a combination of the pelvic ligaments, it seems to me, is not physically or anatomically true. Except during pregnancy, the pelvic ligaments do not act as stays or supports, as we have been so long taught. Personally, I have never observed, save during pregnancy, the round and associated ligaments, especially the round ligaments, to act other than in a simple passive capacity. Fothergill states: "Though all the ligamentous structures attached to the uterus, except the cervicopelvic muscle bands, be severed, the organ will remain in the so-called normal position."

Usually the round ligaments are observed as two cylindrical or ribbon-like cords passively traversing the sides of the pelvis from the internal abdominal rings to the uterine coruna. Rarely are they seen in a state to imply that they in any way act as a sustaining force of the uterus.

It is commonly assumed that a great variety of symptoms may be caused by simple displacements, but it is clear that the mere association of symptoms cannot be explained either on anatomic or pathologic grounds, for simple displacements are not pathologic. Unless

the displacement is frankly complicated it cannot excite symptoms. If one could accept the hypothesis that a simple displacement of the uterus inhibits the supreme function of the organ, namely, childbearing, then one might assume that our Creator adopted this as one of the chief methods of exterminating the human race.

Except in very rare instances, an uncomplicated displacement cannot possibly interfere with conception or any other function. If this were the common source of female sterility, the condition would be infinitely more frequent than it is. Indeed, it may not be far of the mark to say that 25 per cent or more women of the childbearing age would be found in this class.

Personally, I am familiar with no data which prove that simple retrodisplacements bear an etiologic relationship to sterility. In all our literature reference is made to this subject, but there are no data on which one can base a positive conclusion. Sterility is often cited as a sequel of retrodisplacements, but rarely is the story fully told. There is a vast difference between a one-year, two-year, three- and five-year sterility. Simple displacements must play but a minor rôle in the barrenness of women.

While sterility is usually set forth as one of the symptoms of retroposed uteri in one paragraph, the paradox of the possibility of abortion taking place is mentioned in the next.

That this unfortunate termination of pregnancy may take place in uteri imprisoned underneath the sacral promontory, no one will deny, but pelvic incarceration of a gravid uterus is an exceedingly infrequent occurrence. In an experience extending over a period of several years, I have not observed this combination of conditions.

With regard to the teaching, more or less prevalent, that, if pregnancy should occur, a simple displacement might jeopardize the fate of the embryo by expelling it prematurely, is, I am convinced, a species of gynecologic pedagogy not wholly true. Abortion occasionally may occur, just as it does occur occasionally under entirely normal circumstances, but that it is a common cause of abortion, I regard as exceedingly doubtful.

Impaction with abortion as a sequel is possible, but how often has it been observed? The "danger" to a pregnancy complicating a simple displacement is overemphasized. In this connection, I hesitate to use the word "coercion," but I do know the term in the form of a method is sometimes employed in impressing a patient with the "seriousness" of the trouble and I regret to say it also occasionally is used in equally impressing a patient with the "necessity" of surgical interference. The magnitude of the symptom complex, so frequently ascribed to retroposition of the uterus, to me, seems incredulous and cannot be explained on rational grounds.

Indeed, nearly every conceivable symptom, as nervousness, functional and even organic; sterility, leucorrhea, disturbed menstruation, dyspareunia, irritation of the bladder and bowel and, of course, the Nemesis of all women, backache, is often attributed to simple uterine displacements.

Chipman quotes La Rochefaucold, who said: "Pain is the greatest liar in the world," and Chipman goes farther, asserting that, of the painful liars extant, "backache is the greatest Ananias or Sapphira of all."

The men propounding this threadbare doctrine ostensibly believe with the ancients that the uterus has the unusual facility of sailing about like a rudderless ship, ultimately anchoring itself in some favored section of the body.

The teaching is utterly false and the party to benefit thereby is obviously not the patient, but the individual who unscrupuously lends himself to such an iniquitous system of medical banditry—a system which:

"May have heaven in its looks,
But hell in its name."

It is taught, too, by men who I am confident know better, but taught nevertheless, words—words:

"In each of which the teacher shakes a lance,
Though brandished in the eyes of ignorance."

I am fully conscious of the feeling respecting the current of thought encircling the topic of uterine displacements. I realize, as I am sure you all do, that there is still a wide diversity of opinion concerning all features of the subject.

Unanimity of opinion has not crystallized regarding the symptomatology and treatment of displacements and perhaps it never will. But unanimity of opinion rarely applies to anything and it would be obviously unnatural to expect a unanimous judgment with regard to this phase of gynecology.

In this country two interesting papers have recently appeared, one by Dr. Arthur Dean Bevan, if not wholly condemning, advocating at least a reversal of our attitude with respect both to the symptoms and treatment of backward displacements. The other paper, analyzing all features of the trouble and advocating a more compromising attitude, indicates that its author, Dr. George Gray Ward, Jr., believes that certain displacements are influential in exciting symptoms and that in these, surgery is not only justifiable, but successful.

In England, too, at the recent meeting of the British Medical Association, at Bath, a lengthy paper was presented, depicting and ascrib-

ing a long chain of symptoms as due to simple backward displacement. In this contribution surgical therapy was strongly advocated, but in the lengthy discussion which followed, the contentions of the contributor were not supported. By the various gentlemen who took part in the discussion, ten in all, a middle course was advised. In therapy, surgery was given second place.

Bevan in his paper, to which I have already referred, expresses his convictions regarding displacements in the following language: "Thirty years or more ago, as a young surgeon, I was very skeptical about the local and general symptoms ascribed to retroposition of the uterus. I could not understand how a movable retroposed uterus could excite symptoms any more than a mobile sigmoid which might fall backward or forward or right or left. I soon found that patients upon whom I operated and brought the uterus forward in the supposed normal position, were not only not benefited, but many were made worse by the operation, so I, therefore, early discarded it as unnecessary and illogical."

Looking upon this problem, he says, as a piece of scientific research, we are in a position today to state that uncomplicated, movable retroposed uteri produce no symptoms and that operative procedures on such cases must emphatically be condemned.

The retroversion question has also been clearly set forth by Jaschke. In a study of 1000 cases of retroposition, compared with 1000 cases of anteposition, this observer found that the supposed characteristic symptoms of retroposition: menorrhagia, leucorrhea, dysmenorrhea, constipation, bladder irritation, backache, and sterility, occurred just as often in the anterior as they did in the posterior position.

Jaschke has reached the conclusion, therefore, that an uncomplicated retroposed, movable uterus causes no characteristic symptoms of any kind and no characteristic distress.

Realizing that my paper is dedicated to an analysis of uncomplicated retrodisplacement of the uterus, it may not be regarded as apropos to even mention that insignificant entity, if really an entity at all, antedisplacement. It would be a fatuous waste, indeed, of priceless time to even attempt to review the multiplicity of symptoms and the mammoth therapeutic pyramid erected to the glorification of this pigmy of gynecologic deities.

Personally, I do not believe a simple antedisplacement, one regarded as beyond the so-called natural anteflexion, is capable of exciting symptoms.

A pin-hole os I have never seen, nor have I ever observed a cervical canal, the channel through which the menstrual fluid makes its exit from the uterine cavity, with a diameter less than the diameter of a red or white blood cell. Menstrual symptoms associated with ante-

position must, therefore, be looked for in structures other than the uterine body.

The train of symptoms often ascribed to an acutely anteflexed uterus is most frequently found associated with the type of organ classified as the infantile variety. This is most commonly observed in individuals who present anything but infantile characteristics. These patients, on the contrary, are, in the main, of the gigantic type. This feature in itself clearly indicates that the source of the trouble is not in the uterus, but in some derangement of the endocrine system. Herein lies the origin not only of the maldeveloped uterus, but of the dysfunction, expressed symptomatically in dysmenorrhea, partial or absolute amenorrhea and sterility, as well as the bearded face, masculinity, moderate or mammoth body development combined with an anteposed, ill developed uterus; these form a symptom and sign complex which speaks with plain intelligence of the fountain head of the trouble.

It is a common observation that the bigger the patient the smaller the uterus and the more profound the functional derangement.

Treatment.—I have devoted considerable time to the general discussion and symptomatology of simple uterine displacements, because I believe the study of these phases of the subject is more important than the treatment of the displacement itself.

In considering the therapy of simple displacements, while it may shelter one from argument, if not criticism, by assuming a compromising middle course, I shall steer clear of compromise, because I believe, except in very rare instances, a *simple displacement of the uterus is not worth treating.* As Goldsmith said of Burke: "I select this course not because it is expedient, but because I regard it as right."

A study of events discloses that the round ligament operation, a consuming epidemic procedure a few years ago, is now being employed only sporadically.

The late Dr. Watkins said: "The round ligament operation seems to have ceased to be a subject of much general interest."

I am sure we are all familiar with the conservative trend in the treatment of simple displacements and this does not indicate that the trouble is less frequent, but that a mature surgical conscience has discovered therapy is rarely necessary.

Indeed, if the conservative plan gradually evolved and adopted during the past few years could be regarded as a criterion of the future, it is obvious that uncomplicated cases will be treated, if treated at all, along ultraconservative lines. It is probable that simple malpositions will be regarded more from a physioanatomic and

not from a pathologic standpoint. Today the round ligament operation in uncomplicated cases, I rarely recommend or perform.

The only type of displacement which one may legitimately place in the category of a surgical displacement is the large hyperplastic uterus, or the large chronically inflamed adherent uterus or the pathologic prolapsed uterus. In these, considerably more surgery than simply shortening the round ligaments or fixing the uterus forward is called for.

The practice of major surgery for a minor condition is not good surgery and it is prudent to keep in mind that all forms of surgery exact a definite toll of human life.

If one may regard a multiplicity of therapeutic measures as sound evidence that none are wholly satisfactory, then at least some of those designed for simple retrodisplacement may be included in that chapter. More than 100 different operative methods have been devised and next to the pernicious operation of dilatation and curettement, I am not familiar with any that have had less justification or done less good. Ten years ago the round ligament operation constituted more than 10 per cent of the work of the gynecologist. I am persuaded that today it could be reduced to less than 2 per cent and all that is needed to see the consummation of this belief is a righteous surgical conscience. In simple cases it may be used occasionally as a matter of expediency in the course of other pelvic work, but rarely as a matter of principle or on primary organic grounds.

As regards the therapy of anteflexion, I have very little to say. To me it seems physically impossible to correct an ill developed anteposed uterus by either medical or surgical means.

Personally, I believe a grossly maldeveloped anteflexed uterus will remain maldeveloped and probably anteflexed forever, irrespective of any type of treatment.

So far as therapy is concerned, uteri of this form might legitimately be placed in the category of incurable conditions.

If, however, the ill development is of moderate extent, some good may be accomplished by a restricted dietary regime, combined with the administration of organic drugs. Apart from these measures, and even they afford but slight encouragement to either the patient or the physician, there is little one can do.

Surgery in the form of dilatation and curettement alone or combined with a uterine stem pessary or the various mutilating operations on the cervix itself, may occasionally provide some comfort, but surgery, too, generally is disappointing, is not without features inimical to the integrity of the cervical mucosa and indeed not without danger even of a more serious character.

The stand I have taken respecting the symptoms of uncomplicated displacements of the uterus, I realize fully will not meet with universal approbation. It perhaps, on the contrary, will be greeted by condemnation, but I do believe I have expressed a conviction which is gradually becoming and is destined to become more and more universally recognized.

I may be accused also of taking an ultra pessimistic point of view regarding the surgical therapy of simple displacement, but I feel justified in assuming a discouraging attitude because it is sustained, first, by the decreasing frequency with which operations are being performed; second, by the almost universal condemnation of surgical means, and third, by the almost uniform failure in my hands of operative treatment affording symptomatic relief. Two hundred years ago Alexander Pope in his *Essay on Criticism* said:

> "'Tis hard to say, if greater want of skill
> Appear in writing or in judging ill;
> But, of the two, less dangerous is the offense
> To tire our patience, than mislead our sense.
> 'Tis with our judgments as our watches, none
> Go just alike, yet each believes his own."

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(*For discussion see page* 134.)

AIR INSUFFLATION OF THE TUBES*

By Peter Graffagnino, M.D., New Orleans, La.

FOR more than two years the Rubin method for the determination of tubal patency has been used in our clinic at Charity Hospital with such good results that a brief description of the technic and indications is warranted at this time. In the beginning our apparatus was that originally described by Rubin, carbon dioxide gas being the insufflating agent, and his technic was followed in practically every detail. Recently, however, we have modified the method somewhat, with the idea of making possible a wider application, and making its employment practicable not only in the operating room but also in the physician's office or even the patient's room. As shown by the illustration, we have simply substituted the air bulb of the blood pressure apparatus for the carbon dioxide tank, thereby making the apparatus portable and simplifying the entire procedure very markedly.

We believe that this method should be utilized in every instance in which the cause of a woman's sterility is of doubtful origin, and certainly before operation of any sort is ever attempted for the relief of the condition. Our principal indications are:

1. To determine the patency of the fallopian tubes in cases of sterility.

2. To determine the patency of the fallopian tubes as an indication of their involvement in chronic pelvic inflammatory disease or other pelvic pathology.

3. To assist in keeping the tubes open following conservative operative procedures.

4. To determine the ultimate success of operative procedures for opening occluded tubes.

By using this modification of the Rubin apparatus we have found that the following important details of technic can be controlled and a maximum amount of information be obtained from the examination:

1. A constant low pressure of gas or air can be maintained automatically.

2. The rate or flow of the insufflating agent can be regulated accurately.

3. The volume of gas or air which passes into the abdomen can be measured by the siphon meter.

4. Intrauterine pressure can be recorded by means of the mercury manometer.

It should be emphasized that patients are never examined in the

*Read before the New Orleans Gynecological and Obstetrical Society, Meeting of February 18, 1926.

presence of purulent or bloody vaginal discharges, nor is examination ever attempted in patients who have acute pelvic inflammatory disease or serious organic disease, particularly cardiac lesions.

The examination is made under the most rigid aseptic precautions possible. After the patient has been placed in the lithotomy position, and the cervix and vagina have been carefully cleansed, the cervix is exposed by the use of a weighted or Sims speculum, and the cervix and cervical canal are painted with 3½ per cent tincture of iodine. The anterior lip is grasped with the vulsellum, the uterine canal measured with a sound, and the direction of the fundus noted. The rubber tip of the cannula is now adjusted to the size of the canal; the cannula is introduced, and the rubber tip fitted as snugly as possible against

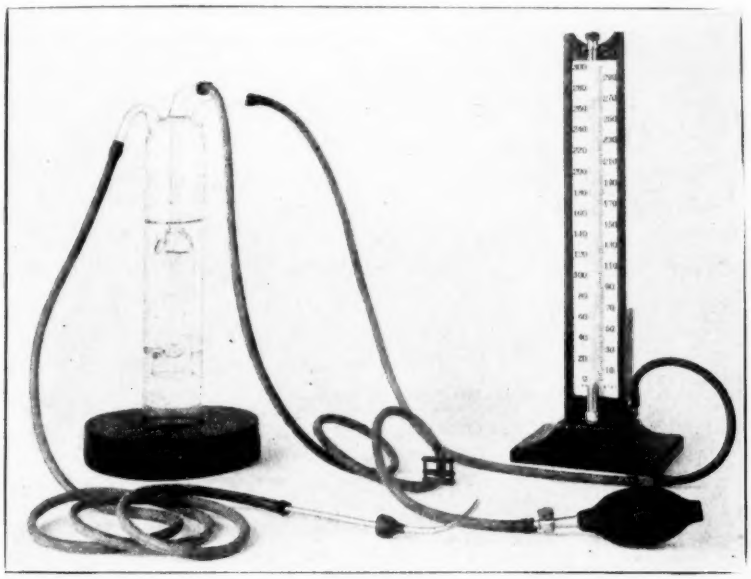

Fig. 1.

the cervix to avoid the escape of the air. The apparatus is now adjusted and connected, and the air allowed to flow gently, so that it will take about twenty seconds for the column of mercury to rise from zero to 100 mm. The volume of air which has passed into the abdomen can easily be measured by counting the number of pulsations or excursions of the air in the siphon meter, about 40 c.c. of air passing into the abdomen with each excursion. Not more than 300 c.c. of air should be introduced when the modified Rubin apparatus is used, because air is not so readily absorbed, often remaining more than forty-eight hours, so that very distressing pressure symptoms may ensue, particularly if the patient is in any way active. Carbon dioxide, on the other hand, is absorbed so rapidly from the abdomen that the symptoms from the

amount used in an average examination will disappear within fifteen to thirty minutes.

If the pressure findings indicate any degree of obstruction to the passage of air through the tubes, too much reliance should not be placed upon one examination, nor is the result of an examination reliable when the patient is near her menstrual period. Examination should not be done within a week before or a week following a period, as the congestion of menstruation may cause partial or complete obstruction of the tubes, and even in a patient whose periods are ordinarily regular some irregularity of time may be present. For some reason, which we have not yet been able to fathom, occasional cases will be found to have occluded tubes at one examination which are patent at subsequent examinations. If we find the tubes obstructed at one examination and can find no definite cause for the obstruction, we examine the patient at least twice more, on different occasions, before we make a definite statement as to the patency of the tubes.

There are three ways of knowing whether or not the air has passed into the abdomen:

1. Pressure findings. A drop in intrauterine pressure during the examination, if there has been no leak about the cannula in the cervix, means that air has passed through one or both tubes. An intrauterine pressure of 200 mm. on repeated trials indicates that both tubes are closed.

2. Shoulder pain. As soon as the patient assumes the upright position she may have pain in one shoulder or both. This symptom we have found to be present in over 90 per cent of the cases in which the air has passed into the abdomen, and we therefore accept it as practically positive evidence that the tubes are patent.

3. Fluoroscopic examination. If the patient is examined in the upright position after the air has passed into the abdomen a layer of the air can easily be seen beneath the diaphragm. At first we routinely subjected all our patients to fluoroscopic examination, but this was later discontinued, and we now fluoroscope only those patients in whom shoulder pain does not develop, particularly if a drop in pressure has occurred.

Most patients complain of some discomfort during the examination, and the shoulder pain, to which reference has been made, in some instances is quite severe. If they are taken into a dark room for fluoroscopic examination a certain number will faint as a result of the shoulder pain and apprehension.

That the method has some therapeutic value, as well as a definite diagnostic value, is beyond question. Various writers have reported cases of pregnancy following simple insufflation of the tubes in undoubtedly sterile women, and it is perfectly possible that the entrance of the gas or air into the tubes, under pressure, will expel mucous

plugs from them, separate agglutinated surfaces, and straighten out kinking which may have taken place along their course. In our hands, however, the procedure is largely a diagnostic one, and it is from that standpoint in particular that we commend it to you.

CONCLUSIONS

1. The modified Rubin method for the determination of tubal patency is a simple and safe diagnostic procedure, the portable apparatus being its principal advantage.

2. If details in technic are carefully observed, an accurate opinion as to the condition of the tubes can be given in at least 85 per cent of the cases examined.

3. Patients should not be examined near a menstrual period, or in the presence of acute pelvic inflammatory disease or serious organic lesions, especially heart disease.

4. All cases of sterility in which a definite diagnosis of the cause cannot be made by bimanual pelvic examination should be insufflated.

5. The method is almost entirely diagnostic, although it has some therapeutic value, and pregnancy will follow in a small percentage of the cases.

PHYSICIANS' AND SURGEONS' BUILDING.

(*For discussion see page* 135.)

SARCOMA OF THE STOMACH*

BY GEORGE F. CHANDLER, M.D., F.A.C.S., KINGSTON, N. Y.

ON JUNE 12, 1923, a woman thirty-eight years of age, the mother of four children, whose last child was born thirteen months before, came to my office for an examination. She stated that she was pregnant and asked advice as to when she should enter the hospital for her next child. She was pale and so weak that every effort exhausted her. She had been vomiting for nearly six months, perhaps once a week at first, with gradually increasing frequency. There was no blood in the vomitus. She thought at times that she had felt quickening but was not sure. Her menses had never appeared since her last child, and she was therefore at a loss to know how far pregnant she was.

Upon examination I found the uterus normal, but found a large tumor in mid-abdomen, which simulated a pregnant uterus. The mass was round, filled the abdomen, and was movable, but did not seem to be attached to anything. It seemed softer than a fibroid. I was sure it was not an ovarian cyst. It was not connected with the liver or spleen, and as she was so emaciated, I could feel each kidney. I felt that she was entitled to an operation since the tumor was movable.

She entered the hospital the next day, and the morning following I opened the abdomen. The mass was of bluish color shining through the omentum. On lifting up the greater omentum, I found that the mass was in the lesser sac of the peritoneum, pulling down the stomach and stretching the gastrocolic omentum. I

*Read at the Thirty-eighth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 16, 17 and 18, 1925.

opened the lesser sac through the gastrocolic fold just to the right of the colicamedia artery, and expressed from the lesser sac a tumor practically round, eight and one-half inches wide by nine and one-half inches from above downwards. It weighed nearly nine pounds; it was solid, attached to a broad pedicle about two and one-half inches wide, and the thickness of a finger. It was attached to the greater curvature of the stomach posteriorly.

The patient's condition at this time was very bad.

I rapidly clamped the pedicle with curved clamps that followed the symmetry of the greater curvature and tied off large vessels individually in the stump, then removed the clamp and covered in the stump with a running suture. A running suture closed the omentum, and a rapid closure of the abdomen followed without drainage.

We despaired of the patient's life for six days, when she began to gain, and finally, much to our surprise, made a recovery. She is today, after two years and three months, a well, strong woman who has gained twenty pounds and says that she has never felt better in her life.

The pathologist reported that the growth was a small, round-celled sarcoma.

Sarcoma of the stomach is one of the rarest conditions presented to the surgeon. According to W. D. Haggard, Bruch in 1847 put on record the first case of primary gastric sarcoma, and Virchow in 1887 operated upon the first patient for this condition. Up to 1912 there were but 61 reported cases with eleven survivals after operation, ranging from three months to seven and one-half years.

In 1914, Flebbe collected 157 cases based on autopsy findings. There had been up to 1920, according to Haggard, but 107 operative cases. Therefore, the total recorded cases of sarcoma of the stomach, up to 1920, of autopsy or operative cases are 244. Since then, I can find only 19 published articles on this subject in this or in any other country, totaling not over thirty more cases. A condition that totals but 274 reported specimens (operative and autopsy together) must be a rare one.

The largest case on record is one presented by Cantwell in which the tumor weighed twelve pounds. Pagenstecher records one weighing eleven pounds. These two cases are the only ones that I can find in which the tumors were larger than that of my own case.

The sex of the patient has no bearing on the frequency of the lesion, it being equally divided. The age limit is from three years to eighty years, but the most common age is 41.6 years, differing from carcinoma, which is 61.2 years, according to the last U. S. Census reports.

There are three groups of cases, viz.: spindle-cell myosarcoma, lymphosarcoma, and miscellaneous round-celled sarcoma.

Douglas states that round cell and lymphosarcomata increases more slowly in size than spindle cell, and judging from the statistics of the progress of the disease, cases of sarcoma of the stomach metastasize less rapidly than carcinoma, and the length of life after the appearance of the disease in nonoperative cases appears to be longer than in carcinoma cases. Therefore operative results should afford a better prognosis than in carcinoma.

It would seem that a benign tumor of the stomach may exist for years, and then gradually become a sarcoma. One such case has been reported by Kimpton where

he resected the stomach for a round-celled sarcoma at the age of thirty years. The patient had noticed this tumor since she was eleven years of age, which case would seem to prove this. These tumors metastasize much less rapidly than do carcinomata. When metastasis does occur the lymph nodes of the stomach are first affected and then the liver, but the general tendency is not to metastasize.

Forni reports that round-celled make up two-thirds of all gastric sarcomata: spindle-celled, less than one-third, and lymphosarcoma, a small percentage.

Ulceration seems to be rare as a rule in this class of tumor, and as the site of the tumor is near, but not commonly in the pylorus, there is less obstruction than in carcinoma.

Early diagnosis with successful removal means a much better prognosis than in carcinoma for this reason.

Overton's patient lived ten years after operation; Krause's patient lived seven and one-half years; Kimpton's five years and ten months; the Mayo's four years, and Douglas of New York has written me that, out of his three cases of this condition, the one that lived was well and healthy six years and six months after operation.

The diagnosis is often impossible. There may be no gastric symptoms at all. The loss of flesh is marked and there is anemia, weakness and frequently hemorrhage from the stomach or in the stools. There is rarely obstruction, as in carcinoma, and the tumor is usually much larger.

I did not use the x-ray nor the fluoroscope, but I believe that the fluoroscope should be used. I doubt if the x-ray would be of much advantage.

NOTE: Since writing this article, I have found five additional cases of Sarcoma of the Stomach noted in The Surgical Clinics of North America for August, 1925, v, No. 4.

11 EAST CHESTNUT STREET.

(*For discussion see page* 122.)

THE INTRAVENOUS MAGNESIUM SULPHATE TREATMENT OF ECLAMPSIA*

A Collective Report of 142 Cases

By E. M. Lazard, M.D., F.A.C.S., John C. Irwin, M.D., and John Vruwink, M.D., Los Angeles, Calif.

(From the Obstetrical Department, Los Angeles General Hospital)

IN OCTOBER, 1924, one of us (Lazard, American Journal of Obstetrics and Gynecology, February, 1925) reported to the Los Angeles Obstetrical Society, the results in a series of twenty cases of eclampsia treated by the intravenous use of magnesium sulphate at the Los Angeles General Hospital. In May, 1925, we were appointed a committee of the Los Angeles Obstetrical Society to collect and report on all available cases which had been treated by this method. We have now records of 142 cases, reported from hospitals and doctors in and around Los Angeles; a few being reported from more distant points.

Most of the cases were from the Los Angeles General Hospital and of the others, many were either under the immediate charge of or were seen in consultation by members of the obstetrical staff of the Los Angeles General Hospital.

We have to thank the managements and staff doctors of the Methodist, California Lutheran, Hollywood, Kaspare Cohn, White Memorial, Florence Crittenton Home, St. Vincent's Maternity Hospitals, and the several doctors who personally reported cases to us, for permission to include their cases in this report.

For purposes of this study, we have included under the term, "eclamptic toxemia," all toxemias of pregnancy which have resulted in convulsions or, in which treatment has been directed toward the prevention of convulsions (preeclamptic toxemias). These cases naturally fall into three classes from an etiologic standpoint.

(1) The true eclampsia (so-called, for the want of a better term) in which the toxemia is the result of some primary toxin, incident to the pregnancy and to which there is added toxemia of liver deficiency and of kidney deficiency (toxic nephrosis). These cases can only be differentiated from the second class by the absence of antecedent history of renal disturbance, by the practically normal blood chemistry and, in case of recovery, by the comparatively rapid return to normal of blood pressure readings and urinary findings; in case of death, by the typical liver changes and lack of any chronic renal changes.

(2) The nephritic eclampsias, which are merely nephritic uremias of the pregnant; these cases are differentiated by the history of antecedent nephritis, the long

*Read at a joint meeting of the Los Angeles Obstetrical Society and the Los Angeles County Medical Association, February 18, 1926.

continued high blood pressure and albuminuria before the onset of eclampsia, by the high values of retention products in the blood, by the comparatively few eclamptic seizures (unless there be complete anuria) and the prolonged uremic coma and delirium; in case of recovery, by the persistence of high blood pressure and urinary evidence of nephritis, by the tendency to recur with succeeding pregnancies, and in case of death, by the autopsy findings of chronic nephritis with few or no liver changes.

(3) That class of cases in which there is superimposed on a mild chronic nephritis, a true eclamptic toxemia.

Preeclamptic Toxemias.—There have been 45 cases, 23 General Hospital and 22 outside cases of toxemia which have received intravenous magnesium sulphate, in addition to the usual preeclamptic treatment, in an attempt to prevent the occurrence of eclampsia (convulsions and coma). Of these cases, nine were given their first injection during labor and three had their first injections postpartum. These were given as prophylactic doses because the patients had high blood pressure, 150 to 240, all but one had albuminuria and casts, and all had headache or edema or both. Thirty-three were started on the treatment from one day to four weeks antepartum; coming under treatment as preeclamptic cases. They received doses of from one injection of 20 c.c. to 24 injections of 20 c.c. each, this last one over a period of twenty-three days.

Of the forty-five patients, six developed convulsions, four of whom had had but one injection, one had had four injections and one had had three injections. In two patients, the convulsions (Cases 2 and 5) developed within twenty-four hours of the beginning of the treatment, in one patient (10) forty-eight hours after her only injection (not given enough), one patient (22) on the sixth day postpartum after having been given one injection at time of labor, and one patient (45) had her only convulsion postpartum after being under treatment for two weeks, antepartum.

Of these 45 patients, 30 had spontaneous deliveries; three, induced labors; five, assisted labors (forceps or version) and seven had cesarean sections. Of the babies, there were 34 living babies, 6 premature stillbirths and 3 full-term stillbirths. One of the full-term stillbirths was due to a premature separation of the placenta.

One patient, (14) a primipara, was referred by her doctor to the General Hospital, for emptying of the uterus because of her toxemic condition at the thirty-fourth week of her pregnancy. She was carried four weeks to spontaneous delivery of a living baby without the occurrence of convulsions.

Two patients were treated in two pregnancies for toxemia. One patient, Case 8, was admitted 4/10/25 as a preeclamptic. This was the same patient as Case 6 of the eclamptic series, who was in the hospital 7/14/24. On her first admission, she was in convulsions when admitted, was given magnesium sulphate intravenously, and the next day delivered spontaneously a stillborn child, making a good recovery. On her second admission, nine months later, she was eight months pregnant, had

a blood pressure of 240/132, albumin ++; she was again given the magnesium sulphate intravenously, and four days later, delivered spontaneously a living baby. She had no convulsions and made a good recovery. This was probably a nephritic toxemia.

This patient, Case 4, admitted 12/20/24, a nephritic with marked general edema, albumin ++++ and casts, had six intravenous injections, a bag induction on 12/31/24 with spontaneous delivery of a premature stillborn child, returned to the hospital 11/8/25. Another patient, Case 21, five and a half months pregnant, with marked generalized edema, blood pressure 190/150, albumin ++++, casts +++, had six injections of magnesium sulphate, with little effect on the general condition, except that she did not develop convulsions or coma, she had a bag induction on 11/12/25. The next day, there being no response to the bag insertion, it was removed and the resident physician dilated manually sufficiently to deliver the five and a half month stillborn fetus. In the manipulation, the very edematous cervix was lacerated but with little apparent bleeding at the time. Two hours later, the patient was in shock and died four hours after delivery. The autopsy revealed marked subacute nephritis, extensive laceration of cervix into base of right broad ligament and extensive hemorrhage into retroperitoneal region of pelvis around vagina and cervix. Liver was very pale with central hemorrhages. Cause of death: subacute nephritis with pregnancy. Contributory shock following laceration of cervix (Maner).

Eclamptics.—In the eclamptic series (those who had one or more convulsions) there were 103 patients, of whom 54 were General Hospital patients, and 49 outside ones, their ages ranging from twelve to forty-four years. Of these 103 patients, there were 69 primiparae. There were 50 antepartal, 25 intrapartal and 28 postpartal eclampsias.

Mortality.—There were fourteen deaths from all causes in the entire series, a gross mortality of 13.6 per cent. Cases 3 and 19 were early cases and did not have the treatment which is carried out at the present time. They were reported in detail in the preliminary report (AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, February, 1925).

CASE 22.—This patient recovered from her eclampsia, had a spontaneous delivery of twins, developed a puerperal sepsis from which she died three weeks postpartum.

CASE 25.—A primipara at her eighth month, had one convulsion, went into coma from which she did not come out, and died eighteen hours later without having any more convulsions. It was our impression that she had a cerebral hemorrhage but no autopsy of the brain was made. The autopsy showed typical eclamptic changes in the liver.

CASE 31.—Patient admitted in coma, had a spontaneous delivery of twins, had no convulsion after admission, and died forty hours later. Autopsy showed *no* eclamptic changes in liver, subacute nephritis, localized areas of bronchopneumonia, pulmonary edema.

CASE 33.—This patient, para x, eight months pregnant, had three convulsions fourteen hours before admission and remained in deep coma. On admission she was profoundly comatose; there were evidences of bronchopneumonia and pulmonary edema; she died twelve hours after admission, undelivered. *Autopsy*: confluent bronchopneumonia, fatty infiltration of liver with diffuse hemorrhagic areas in lobules, cloudy swelling of kidneys.

CASE 36.—Para i, eight months pregnant. Convulsions began three hours before admission and were not controlled until seven hours after admission; constantly deepening coma, patient died, undelivered, twenty-four hours after admission. *Autopsy:* confluent bronhcopneumonia of upper and lower lobes of right lung, usual eclamptic changes in liver, acute parenchymatous degeneration of kidneys.

CASE 46.—Para i, six and a half months pregnant, first convulsion two and a half hours before admission; second convulsion one hour later, she was admitted in coma. No further convulsions. Came out of coma partially the first day, then with gradually deepening coma, she died, undelivered, five days after admission.

Clinical Diagnosis.—Nephritic uremia. No autopsy.

CASE 55.—Para ii, six months pregnant. Convulsions began ten hours before admission, ten convulsions having occurred; she was in coma on entrance, had one convulsion after first injection of magnesium sulphate, remained in coma, presented evidences of cerebral injury and of bronchopneumonia. Died, undelivered, twenty-seven hours after admission.

Clinical Diagnosis.—Nephritic uremia. No autopsy.

CASE 76.—(Outside case) Para i, eight and a half months pregnant. Admitted in posteclamptic coma, having had one convulsion; no further convulsions. Coma completely cleared in twenty-four hours. Cesarean section sixth day after recovery from eclampsia; she went into shock on table and died one hour later of surgical shock.

CASE 77.—(Outside case) Para i, eight months pregnant. Patient was admitted to hospital in labor. She developed intrapartal eclampsia, had a spontaneous delivery, death occurring four hours later, without any more convulsions. *Autopsy:* typical liver changes, severe acute renal degeneration.

CASE 79.—(Outside case) This patient was admitted in coma. Twin delivery nine hours before entrance. Convulsions began six hours after delivery. Last convulsion five hours after admission. Did not come out of coma and died thirty-nine hours after admission. Had considerable treatment other than magnesium sulphate.

Clinical Diagnosis.—Nephritic uremia. No autopsy.

CASE 85.—(Outside case) Para i, at term. She drank excessively of alcoholics (bootleg) during pregnancy. Forceps delivery; six hours later, convulsion, almost complete anuria first twenty-four hours; came out of coma within twelve hours, then low delirium; three and a half days later another convulsion, coma for six hours, then low delirium. She died eight and a half days after delivery. Showed high retention products values in blood chemistry.

Clinical Diagnosis.—Nephritis. Autopsy showed *no* liver changes; pyonephrosis, chronic interstitial nephritis with an acute hemorrhagic nephritis superimposed.

CASE 94.—(Outside case) Para i, at term. Coma and convulsions two hours before entering hospital. Spontaneous stillbirth one hour after admission. Only two convulsions in hospital, the last one, nine hours postpartum. She did not come out of coma and died three days after admission. Very high retention products values in blood chemistry.

Clinical Diagnosis.—Nephritic uremia. No autopsy.

Of these fourteen patients who died, one (22) recovered from her eclampsia, and died three weeks later from sepsis, and one (76) died

of surgical shock from section, six days after recovery from eclampsia. These two cases should be figured as recoveries from the eclampsia. One patient (33) was moribund when she first came under observation, and two (31 and 85) were proved, by autopsy, to be straight nephritic uremias without any typical eclamptic changes postmortem.

Deducting these five deaths, there are left nine deaths in one hundred cases, a corrected mortality of 9 per cent. There were four of these nine deaths clinically nephritic uremias, but as there was no postmortem examination, we are including them in our mortality to be on the conservative side. In addition to this, the first two cases were early ones and had much other treatment, which as we have already pointed out, we felt was in great measure responsible for the outcome.

The General Hospital cases in this series naturally show a higher mortality than those from the outside because the latter were for most part private cases which had had some prenatal care, while those from the General Hospital were all what might be termed "neglected cases." Of the fifty-four General Hospital cases, 90 per cent first came under treatment from two to fifteen hours after the beginning of the eclamptic attack and were admitted in convulsions or in post-eclamptic coma. Of these fifty-four, there were eight deaths, a mortality of 14.8 per cent. In the five years immediately preceding the institution of this method of treatment, the mortality rate at the General Hospital as reported by one of us (Irwin, *California and Western Journal of Medicine*, Feb. 26) was 36 per cent. Our mortality rate, therefore, in the first year and a half of this method has been reduced about 60 per cent.

If we include the 38 cases which were definitely preeclamptic when they were first given magnesium sulphate and who did not develop convulsions, we have nine toxemic deaths in one hundred and thirty-eight cases, a corrected mortality of 6.5 per cent for the entire series.

Of the 75 ante- and intrapartal eclampsias, six patients died undelivered, there were forty-eight living babies, sixteen premature stillborn and ten full-term stillborn; eight of the living babies dying of prematurity or toxemias within two weeks, so from the seventy-five patients who were delivered after treatment was instituted, there were forty living babies discharged from the hospital.

In presenting this subject at a clinic at the Los Angeles General Hospital to a group of doctors, one of us was asked, "Doctor, do you carry out this procedure in your private cases?" The answer was, "Certainly, why do you ask?" Whereupon the doctor replied, "The attacks are so terrifying to the family that they constantly importune the doctor to institute some more radical procedure," meaning

by this, a termination of the pregnancy. A study of these deaths will answer this question.

Of the fourteen deaths, two were postpartal cases, one (Case 19) had a difficult forceps delivery at the height of her toxemia, one died of sepsis three weeks after a spontaneous delivery, one had a spontaneous delivery of twins immediately after admission, one died of surgical shock from section after recovery from eclampsia, one intrapartal case died four hours after an easy spontaneous delivery, one (Case 94) spontaneously delivered within an hour after admission. In none of the cases could delay in completing the delivery have been a factor in the fatality, while in one the surgical shock of the delivery was the direct cause of death, and in one, in all probability, it influenced the outcome unfavorably.

Of the six who died undelivered, one remained in deep coma and died eighteen hours after her only convulsion, one was moribund (bronchopneumonia and pulmonary edema) on admisison, dying within twelve hours, one died twenty-four hours after entrance without coming out of her coma, one died on her fifth day in the hospital in a uremic coma, one died in a nephritic uremia, twenty-seven hours after admission.

Surgical termination of the pregnancy, in any of these cases, was out of the question, as it would only have hurried the fatal issue.

As to other treatment, a study of these fatal cases will show that they were the ones which had most supplemental treatment.

Intercurrent Eclampsia.—Lichtenstein describes what he terms "intercurrent eclampsia," in which, with conservative treatment, the eclampsia is overcome and the patient may go from several days to several weeks to delivery without recurrence of the eclampsia. In this series, of the fifty antepartal cases, there were fourteen, 28 per cent, which recovered from the eclamptic attack and went from three days to six weeks before delivery without further eclampsia.

Of these fourteen cases, two were discharged undelivered and reentered the hospital fifteen days and twenty-two days, respectively, after eclampsia, and were spontaneously delivered; four had induction of labor because of persistence of toxemic symptoms (no eclampsia); three had sections (no general hospital case), and five had spontaneous labors.

One case (47) was of particular interest. This patient was admitted to the hospital eleven hours after onset of convulsions, which had recurred hourly during the day; she had been in coma continuously since first convulsion and was at her thirty-second week of pregnancy. Two injections of magnesium sulphate controlled the convulsions and she was carried six weeks without recurrence of eclampsia to the spontaneous delivery of a living baby.

Of the sixty-seven cases delivered after the treatment was instituted, there were forty-seven spontaneous labors, ten forceps extractions, three versions, one breech extraction, eight bag inductions and eight cesarean sections.

There has been but one cesarean section on an eclamptic patient at the General Hospital since we began the intravenous use of magnesium sulphate. This patient (Case 53), para i, had been in labor twenty-four hours before admission, the os was dilated to 4 cm. and the head was high above the inlet of the pelvis. While she was being examined, immediately after entrance, she had her first convulsion. She had three injections of magnesium sulphate before being operated upon three hours later, the cesarean section in this case being done for the dystocia and not because of her eclampsia.

Of the seven outside cases which were sectioned, one (Case 68) was operated upon for a cardiac decompensation, convulsions developing after the operation; one (Case 88) for a preeclamptic toxemia, convulsions developing after the operation; four (Cases 16, 56, 76, 90) after the convulsions and coma were entirely cleared, and one (Case 83) during the eclamptic attack, so that of the eight cesarean sections, only two were done during the eclamptic attack and both of these because of dystocia.

The rationale of the intravenous magnesium sulphate treatment of eclampsia is as follows: As stated in the preliminary report, our first idea was to control the convulsions by the sedative and anticonvulsive effect of magnesium sulphate as was first demonstrated by Meltzer and Auer. "In addition, eliminative measures, such as phlebotomy, stomach lavage, administration of castor oil, colonic flushings with glucose and soda were carried out as in the treatment of any toxemic condition." It was very soon noted that there was apparently a marked eliminative effect, evidenced by the diuresis produced, the rapid subsidence of the edema and improvement in the toxemic condition.

This eliminative effect, we thought to be due to the dehydrating effect of the intravenous magnesium sulphate. The tissue fluids are drawn into the blood stream, thus reducing the edema, and by increasing the aqueous content of the blood, diuresis is increased, overcoming acute kidney block and relieving the toxemia. The coma clears up more rapidly because of the reduction of cerebral edema (intracranial tension). Further experience has confirmed to our minds these deductions.

A study of the case records also seemed to show that where additional eliminative measures (lavage, phlebotomy, hot pack, etc.) were vigorously employed, the convulsions were more difficult to control

and, in two of the General Hospital cases, apparently were factors in the unfavorable outcome.

In this regard, the third conclusion of the preliminary report ended as follows: "However, as our confidence in the magnesium sulphate has increased, we have gradually reduced this supplementary treatment until, in the last two cases, little else was done." Since then, in the treatment of the toxemias at the Los Angeles General Hospital, we have eliminated practically all other measures, depending entirely on the magnesium sulphate. That our confidence was not misplaced is proved, we believe, by the analysis of our cases.

The following routine is posted as a guide for the resident staff at the Los Angeles General Hospital: Preeclamptic cases with blood pressure 150 or higher, in addition to the usual sedative and eliminative treatment and dietary regulation, 20 c.c. 10 per cent solution magnesium sulphate intravenously; blood pressure to be taken twice daily and intravenous magnesium sulphate repeated if blood pressure does not come down. Surgical interruption of the pregnancy only to be done with the consent of senior attending obstetrician. In eclampsia, 20 c.c. 10 per cent solution magnesium sulphate intravenously as soon after first convulsion as possible, to be repeated every hour until convulsions are controlled (attending obstetrician to be notified if convulsions are not controlled within three hours). Blood pressure to be taken every hour after the convulsions are controlled and if blood pressure begins to rise, again nearing its height at time of convulsion, repeat magnesium sulphate; also repeat if convulsions recur.

If patient is comatose or very restless in a semicomatose delirium and blood presure is falling, give chloral hydrate, gr. 20, and sodium bromide, gr. 40, *per rectum*. All patients to be prepared for delivery as soon as they are quiet enough to do so.

Utmost quiet to be observed and nurse to be constantly with patient until coma has cleared. Oxygen inhalations after each convulsion until breathing is normal. If patient is in labor, give nitrous oxide gas for pains. If in second stage labor and proper progress is not being made, low forceps extraction or version may be done with consent of attending obstetrician. *Cesarean section only to be done for absolute obstetric indications and with consent of senior attendng obstetrician.* After patient is delivered, blood pressure to be taken daily and intravenous magnesium sulphate to be repeated as indicated by rise of blood pressure.

All patients on discharge are referred to the medical clinic for thorough examination, in order to eliminate any possible local focus of infection which may have acted as an exciting cause of the eclamptic attack.

Reactions.—The reactions to the intravenous injection of magnesium sulphate have been mild, except in one instance, and all rapidly pass off. The one reaction noted was in a cardiac patient with decompensation, who developed eclampsia after delivery (by section). The doctor reports "severe systemic reaction, cyanosis; short jerky respiration which cleared in about fifteen minutes. No more convulsions." This patient made a recovery.

The preeclamptics all complain of a feeling of warmth when the injection is given; occasionally there is nausea and vomiting, this especially if injection is given shortly after a meal; in a few cases, there were chills folowed by a rise in temperature, in one case to 104° F., all of which rapidly cleared.

In the past year there have been a few reports from other clinics which have used magnesium sulphate intravenously.

H. J. Stollenwerck, of Jacksonville, Florida, in a personal communication, reports six cases in which this treatment was carried out. These cases are included in this series.

J. O. Arnold, of Philadelphia (*The American Physician*, December, 1925), reports the intravenous use of 20 c.c. of 10 per cent solution magnesium sulphate in conjunction with phlebotomy. He reports twelve cases, with recoveries in all.

S. Berman, of the Boston Lying-In Hospital (***Boston Medical and Surgical Journal***, Jan. 7, 1926), says, "We have used the magnesium sulphate solution in several cases and thus far the results have been very encouraging. The patients become restful and the urinary output increases. The convulsions do not cease entirely but come less often. We believe it a worthy adjunct to our present method of treatment and deserving of a fair trial."

CONCLUSIONS

1. Intravenous administration of magnesium sulphate in sufficient dosage will prevent the development of convulsions and will control them after their onset.

2. A series of eclamptics is presented which, under the intravenous magnesium sulphate treatment, shows a corrected mortality of 9 per cent.

3. The true nephritic type shows the greatest mortality.

4. Surgical interference in the eclamptic should be limited to assisting labor (in the second stage) on definite obstetric indications.

5. Cesarean section in the eclamptic is contraindicated except in the presence of absolute obstetric indications.

Our thanks are due Dr. G. D. Maner, Pathologist at the General Hospital, and Dr. A. H. Zeiler for autopsy reports; to the various doctors who reported cases to us or allowed us to review their case records, and to our associates on the attending obstetric staff of the General Hospital for their cooperation in the work.

2007 WILSHIRE BLVD.

BREAST CANCER METASTASIS*

By W. A. Coventry, M.D., F.A.C.S., Duluth, Minn.

(From the Duluth Clinic)

With the year 1919, when the medical literature contained a large number of references to the use of the roentgen rays, both in preoperative and postoperative cases of cancer of the breast, dissatisfied with the results obtained, I began to keep a more accurate record of all cases operated upon by myself as well as by several of my colleagues. We were all of the opinion that possibly the use of roentgen rays would tend to cure, to promote longevity, or to delay the fatal results in cancer of the breast. I frankly state that previous to 1919 I was discouraged with the results. At the present time I am more discouraged at the results of the so-called "cure" of breast cancer cases which have been operated upon by myself and by colleagues. A careful study of these cases has also brought forcibly to our attention the many avenues of metastasis that may occur in breast cancer.

Of the ten women operated upon in 1920, eight are dead and two are living but have recurrences.

Of the seven operated upon in 1921, five are dead; one has recurrences, and one is living and well.

Of the nine operated upon in 1922, eight are dead; none have recurrences, and one is living.

Of the eight operated upon in 1923, two are dead; two have known recurrences; four are living and well.

Of the seven operated upon in 1924, four are dead; three are living; none have recurrences.

Of the six operated upon in 1925, one is dead; four are living; one has recurred.

This totals forty-seven cases in the five-year period. Twenty-eight, 60 per cent, are dead. Four, 9 per cent, are living with known recurrences; fifteen, 31 per cent, are living. Of the fifteen living, eleven were operated upon within a two-year period. Of those in the five-year period all are dead or have recurrences.

All deaths were due to cancer metastasis, except two, one due to lobar pneumonia, which we were unable to prove had anything to do with metastasis, and one due to a long-standing diabetes.

Of those living who have recurrences, carcinoma developed in one

*Read at the Thirty-eighth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, held at Hot Springs, Va., September 16, 17, and 18, 1925.

in the skin on the operated side; in two, in the opposite breast; in two, in the supraclavicular glands of the neck, and in one, in the spine.

Fortunately there are a few still living without any signs of recurrence, but the five-year period has not yet passed for them.

A review of these statistics is not encouraging.

In all of these cases the radical operation was employed with two exceptions. By "radical" I mean removal of the pectoral muscles, major and minor, wide areas of skin and breast tissue, of the fascia down to the ribs and that extending up to the clavicle, of the axillary glands and gland-bearing area. I believe the skill exercised in the removal of these breast cancers was of average type.

Eighty per cent of the cases had a preliminary treatment over the breast and the gland-bearing area in the axilla with roentgen rays, the average dose being five milliamperes, 100 kilowatts, 9 inch gap, 10 inch focal skin distance, 5 mm. aluminum filter, and 15 minute treatment.

Operation was then done at varying periods from two days to one week following the initial radiation.

Ninety-five per cent of all cases have had postoperative x-ray therapy, the treatments varying from two to as high as twelve, in varying periods, from two to three weeks apart. In some, the dose has not been as great as in others, but the standard dose already noted has been attempted. Full treatment was not given those patients who suffered from marked nausea and so-called "x-ray sickness." In fact, this dosage of x-ray was decidedly disagreeable to many of the patients, and it was only by the greatest persuasion, and, of course, the hope that the treatment would be highly beneficial, that we were able to prevail upon many to continue the treatment.

Never before have we observed such apparently rapid metastasis, and metastasis into so many portions of the body as this little study has revealed. Our observations on metastasis have confirmed those of Handley as to the avenues of invasion.

Our series show that 95 per cent had axillary involvement before operative interference. These patients, however, were operated upon, the operator being well aware of the fact that much has appeared in the literature advising against removal when the axillary glands are involved. I am, however, certain that if the axillary glands are involved, one may at least attempt operation. We have observed that in those with axillary involvement that were followed with x-ray treatment, especially into the axilla and over the breast area, only 2 per cent of the patients have had recurrences in the axilla of the side that was operated upon.

There were four cases in which there was metastasis into the clavicular group of glands, either subclavicular or supraclavicular. The more recent literature tells us that these cases should not be operated

upon under any circumstances. Our observations have led us to believe, although we have operated upon these cases, that not to operate is much better than to operate, because these cases in which we have found supraclavicular glands, in spite of the intensive x-ray treatment, have rapidly progressed and shown metastasis elsewhere, as well as in the supraclavicular region.

Metastasis through the chest wall to the mediastinum and lungs has been observed in only two cases. There were, however, cases in which there was lung involvement demonstrated, and whether they were primary through the chest wall, or whether they were due to malignant emboli or metastasis from some other source, we were not able to determine. We had one case, however, in which there was known metastasis through the pleura.

Carcinoma in the opposite breast occurred in two cases of the series, one of these being in a nursing mother.

In four cases carcinoma later developed in the liver, but these were also associated with metastasis to other parts, so we have been unable to determine whether the liver involvement was secondary to the breast involvement, or whether it was secondary to a metastasis that already had taken place in other parts of the body.

Local recurrence in the skin has occurred in only one case. Our observation previous to 1920 showed that local recurrences to the skin occurred comparatively frequently, but I am of the opinion that the treatment with x-ray has undoubtedly retarded the occurrence of metastasis in the scar or in the skin over the removed area.

Metastasis in the skeletal bones, especially the spine, the pelvis, and the heads of the femurs, have been most prominent in this series.

Pain in the hips, in the pelvis, or in the back after an operation for carcinoma, even before definite evidence can be found by x-ray, is a very characteristic sign of metastasis. This pain is very persistent and intense. More particularly is this true in cases of spinal metastasis. The frequency with which metastasis into the skeletal parts has been observed in this series, certainly leaves the impression that our use of x-ray seems to have scattered metastasis to remote parts rather than to have retarded it, as we had hoped it would do.

In the order of frequency, metastasis has occurred in the head of the femur, the ileum, spine, sternum, the ribs, skull, and the lower jaw.

We have not yet seen a case of metastasis in the skeleton below the head of the femur.

The treatment of metastasis, especially of the skeletal parts, by the use of x-ray, has not been satisfactory. Prompt and better results are recorded by the use of the high voltage dosages, when the pain is said to be relieved and the disease somewhat retarded.

Metastasis into the skeletal parts can only be determined by repeated x-ray pictures of the parts suspected of involvement, and in the early stages only by the closest scrutiny.

It is generally agreed that the degree of malignancy in carcinoma is due to the type of cell found in the tumor. Tumor masses showing hyalinization and fibrosis generally speak for longevity, while those cells of a more embryonic type speak for a shorter life. The unknown quantity of the degree of resistance of the patient must also be taken into consideration. These facts have been well shown by McCarthy and Sistrunk in a very admirable work. It is generally recognized that the size of the tumor in the breast is of no particular prognostic value, but that the involvement of palpable glands, with fixation, decreases the chances more than one-half for a favorable outcome.

All of the cases operated upon and reported here have had pathologic examinations by competent pathologists. Those found to be of the scirrhous type have lived longer than those in which there was marked mitosis.

With experience, one comes more to believe that it is much better to give the patient the benefit of the doubt and remove all fibromas and cystic mastitis, so-called "lump in the breast"; this is a much safer procedure than to allow them to remain until a gross diagnosis of cancer can be made.

Also, one may come to this conclusion: In view of the fact that when metastasis has taken place even into the axilla, cancer, although one may operate and use all precautions known, has undoubtedly spread beyond the control of the surgeon, and one cannot help but feel that these patients would be far better off without operation.

Our observations show that, in view of the fact that skeletal metastasis is so common and when once found the prognosis is hopeless, it is better practice in all cases of breast carcinoma to take roentgen pictures of the ileum, head of the femur, and the spine, so as to determine before operation whether there is any metastasis in these parts. If metastasis is found, it would be very much better to refuse operation and to attempt to treat palliatively; I feel sure that the ultimate outcome would be as favorable, if not more so, and that life would be prolonged by such a procedure.

Our observations also convince us that the use of x-ray preoperatively and postoperatively certainly has not shown the results that were hoped and expected of it, when this series began.

(*For discussion see page* 122.)

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D.

THIRD ANNUAL CONFERENCE OF STATE DIRECTORS OF MATERNITY AND INFANCY WORK

Held at Washington, D. C., January 11 to 13, 1926

REPRESENTATIVES were present from forty-one cooperating states and three states not cooperating with the federal and state activities. A program had been arranged by a committee of directors (appointed at the previous conference) working in conjunction with the Children's Bureau. Papers were presented by various authorities in their respective lines, and also by directors who had made a special study of or had valuable experience along certain lines, mostly in regard to the administrative side of the work.

DR. FRED L. ADAIR, of Minneapolis, read a paper on **The Physician's Part in a Practical State Program of Prenatal Care.** (Will appear in the August issue.)

DR. ROBERT L. DENORMANDIE, of Boston, presented the **Standards of Prenatal Care,** intended for physicians in private practice and in clinics. (Will appear in the September issue.)

MISS CAROLINE VAN BLARCOM discussed **The Nurse's Part in a State Program of Prenatal Care.**

The general work of the nurse is to assist the physician in carrying out the prescribed details of supervision, instruction, and care of expectant mothers, and to work toward the ideal of having every expectant mother under medical care from the beginning of pregnancy. She must cooperate with the physician to reorganize and regulate everyday lives of the expectant mothers in his care, and is responsible to him, because all her work is an interpretation and exact application of medical teaching. She must inspire in her patients a confidence which will lead them to follow consistently her advice and instruction on details that the physican wishes them to know about but which he rarely has time to dwell upon for each patient as often and as long as he would like. She is responsible to the community, because her service is of public importance, the future welfare of the race depending upon the aggregate of such work as hers. She should know of the high maternal and infant mortality and the impairment of health of mothers and babies who do not die, both due, to a certain extent, to preventable conditions associated with childbirth. She must know the physiologic changes of the process, the earliest and mildest symp-

toms of danger, and the importance of immediate treatment for them. She must record each observation made at each visit to the patient. If she is to take temperature and blood pressure and do urinalysis, the requirements must be rigid, all symptoms must be noted and reported promptly, and such intangible symptoms as depression, unusual fatigue, even carelessness, as an indication of fatigue, must be observed. The patient must be taught how to care for herself, what changes to expect, what symptoms to note, how to prepare the baby's outfit, and how to prepare for delivery. Most maternity patients are still cared for in their own homes, and demonstration of clothing and other needed equipment is better than verbal description. The nurse's ingenuity may be taxed to help produce the results needed, yet she must remember that the requirements of all expectant mothers are the same, no matter how their financial and social levels may interfere with the attainment of them. Lastly, the nurse must clear up the varied fears and mental obstacles which are in the minds of most patients, and replace them by a joyous anticipation of the baby that is to be born.

Dr. Henry Schultz, of Chicago, read a paper on **Statistical Studies and Graphs.***

Dr. Robert L. DeNormandie read a paper entitled **How to Make a Study of the Causes of Maternal Mortality.**

The international list of causes of death is to be followed, thus including all deaths of women, due more or less indirectly to childbearing.

Not to be classified under the puerperal state are deaths of pregnant women from criminal abortion, an accident which in itself is enough to cause death, long-standing chronic disease, such as tuberculosis or cancer, and acute infectious disease (except influenza).

Whether or not all puerperal deaths are so recorded depends upon the classification made by the attending physician. The word puerperal should be added to the death certificate whenever a death occurs during or following pregnancy. Physicians are not always accurate on this, as appears whenever the deaths within the childbearing age are checked up against the birth returns in a period under study.

From the registrar of vital statistics must be ascertained the woman's name, home address, place of death, certification of cause of death, and the name of the physician in charge. The physician must then be visited and further information sought. For most cases there will be no history, no record of the cause of death, no temperature charts, nothing but the physician's memory, to recall details of a death which may have occurred many months before. If possible, the number, character, and outcome of the woman's previous pregnancies, her past medical history, and the kind of prenatal care received during her last pregnancy should be learned. The kind of delivery, the vaginal examinations made, the technic of the physician, and, for an operative delivery, the length and type of labor, the operation performed, and whether or not pituitrin was used should be ascertained.

Assembling, tabulating, and analyzing these facts should aid in determining where the responsibility for maternal death lies, or, in other words, in determining whether any of these deaths are preventable. Sepsis and puerperal albuminuria cause about 65 per cent of the deaths from childbirth; and the responsibility for sepsis lies with the attendant at delivery in most of the cases.

*This, as well as other papers presented at the meeting, can only be announced by title in the Journal because of lack of space. They may be found in No. 157 of the Publications of the Children's Bureau.

DR. JULIUS LEVY, of Newark, N. J., discussed **Midwife Classes.**

New Jersey, with a population somewhat more than 3,200,000 has about 3,000 physicians, 69 large general hospitals with free clinics, and about 30 small private hospitals and maternity houses, one county having no hospital of any kind. The State Board of Medical Examiners has control of the licensing and suspending and revoking of licenses of midwives. The Child-Hygiene Bureau has been interested in supervising midwives, because this has seemed essential and necessary for the proper protection of child life. The midwives not only attended about 42 per cent of all the births occurring at the time the bureau began work but also exerted a highly important influence upon the survival of the infant, the mother's attitude toward it, and the care to be given it.

It has seemed most economical and efficient to place in a limited area one nurse who would be responsible for work touching all the important factors entering into the life of the child and certain related activities. The next step was to have district supervisors of nurses, each to direct the activities of as many nurses as she could well supervise, and to supervise also the work of the midwives in the respective districts. An assistant in the central organization bears the responsibility for the field work of the district supervisors in regard to midwifery. In 1919 the bureau had one supervisor who covered two counties. In 1925 there were 12 working in the 21 counties of the State. In 1919 there were 946 licensed midwives, of whom 450 were active, and 262 midwives were practicing without a license; they delivered 42 per cent of the births. In 1925 there were 398 licensed midwives and 11 unlicensed (all of whom have been referred to the State Board of Medical Examiners for prosecution), and they delivered 23 per cent of the births. The lower percentage of births delivered by midwives is probably to be ascribed to the restriction of immigration, as well as to their supervision.

In 1919 the midwives hardly knew that the law required them to use silver nitrate in the eyes of the newborn, and cases of ophthalmia neonatorum were frequent. In 1925 it was shown that 98 per cent used this solution, and ophthalmia of a gonorrheal nature is now almost unknown in the State. In 1919 about 32 per cent of the midwives carried a spare bag and equipment. In 1925 good bags with equipment exactly as required by the bureau were carried by 87 per cent. This is a result of inspection of the bag in the home as the midwife uses it. In 1919 it was found that 21 per cent of the midwives carried various instruments and prescribed drugs. In 1925 it is rare that any give a hypodermic or prescribe a cathartic pill. They have learned to read and use clinical thermometers, and 80 per cent used them regularly in 1925. Physicians are called by 77 per cent of midwives for cases showing any abnormality in pregnancy, labor, or the newborn infant, a form for this being supplied.

The district supervisor gives an estimated proportion of one-fourth of her time to the midwife work, visiting the midwives directly, visiting prenatal cases reported to them, and investigating puerperal deaths, infant deaths, and stillbirths in order to have detailed information in regard to midwives' methods.

It has been pointed out to the midwives of Newark that inasmuch as the deaths of infants under one month of age constitute about one-half of the deaths under one year of age, and the deaths under one week constitute about one-fourth of the total, it would be desirable to get a record of the births the day the babies are born. A postal card blank for name, date, and address of the birth, addressed on the other side to the State department, was printed for the midwives' use. The fact that today these cards are being received within twenty-four hours of the birth for about 90 to 95 per cent of all babies delivered by midwives in Newark would indicate what can be done through active cooperation with the midwife.

DR. MARTHA M. ELIOT described a **Demonstration of the Community Control of Rickets.** (This is an important obstetric problem.)

DR. ALICE WELD TALLANT, of Philadelphia, discussed the matter of **Informing the Medical Profession in Regard to Maternal and Child Welfare Work.**

MISS NINA SIMMONDS spoke on **Nutrition in Relation to Reproduction and Vitality of the Offspring.**

It has been noted in regard to humans that a mother producing much milk is not necessarily producing good milk. Unless she has a satisfactory diet her milk is of poor quality. A number of examples were cited. The prevalence of osteomalacia is noted in Manchuria and the Shansi province where the diet is low in mineral content and in vitamine *D*. This is especially common among women during puberty, pregnancy, and lactation, the calcium supply in the bones being drawn upon when the need for calcium salts is greater than the intake in the food. Addition of calcium to the diet does not make good the deficiency; good food, cod-liver oil, and sunlight are needed to aid in its assimilation.

The diets of the pregnant and nursing mothers are of the greatest importance for the well-being of the child, but it is shortsighted to wait until a woman is pregnant before taking note of her diet. Faulty diet may interfere with fertility, prenatal development of the young, secretion of milk of satisfactory quality, and development of skeletal tissues of the nursing young. It may cause in the mother very damaging nutritional disturbances and sometimes extreme and permanent injury.

MR. WILLIAM M. CHENERY read a paper entitled **How Can Popular Magazines Aid in Campaigns to Reduce Infant and Maternal Death Rates?**

An editor must publish what the people will read. If he does not, his magazine goes into bankruptcy, for his mistakes in regard to what the readers wish are revealed in red figures submitted by auditors. All newspapers and magazines operate under this compulsion, the newspapers having the advantage that they can appeal to several audiences, whereas a magazine has but one to which to appeal, and it must calculate on winning the interest of at least 60 per cent of that audience. Consequently any campaign for the reduction of maternal and infant mortality must be related to the interest of large groups of people. In order to do so the campaign must not remain abstract but must be translated into terms of individuals, and be expressed in the story of the fortunes or misfortunes of real or fictional persons in such manner that the reader feels a bond of sympathy. Another method of lesser value is to relate the material to something in which the reader sees utility for himself, as is done, for example, in the service columns of the women's magazines especially, and in newspapers. A third method is the announcing, when possible, of some new principle or general truth containing an element of novelty, such as the idea that poverty has a universal relationship with infant mortality, which seems to be the inevitable conclusion of certain studies in regard to infant mortality which the Children's Bureau made some years ago. Since the great majority of the public do not appreciate the value of scientific work that is being done, or even know that any is being done, there is an actual obligation on the part of the scientific workers to have at least a share of the results of their labors translated into a medium which the general public can understand.

DR. WM. H. DAVIS read a paper entitled **Stimulation of Birth Registration.**

Nearly all the states have good registration laws (12 are not yet in the birth-registration area), but the laws are not well enforced in all. Imperfect enforcement may be due to inadequacy of appropriations for clerical help and field agents to assist state registrars; to carelessness, indifference, or actual hostility on the part of physicians, midwives, and parents; or to the fact that the state registrars may be too lenient and delay prosecution in the hope that persuasive measures will suffice. The lack of a uniform policy in regard to prosecutions is one of the greatest drawbacks to good registration at the present time. In Pennsylvania where, as in many other states, the physician must report each birth within ten days, the child's rights are preserved, even if the physician fails to report the birth; this is done by the requirement that the physician must file an affidavit giving the reason for delay in filing the original certificate and swearing that the facts thereon are true and correct. If he objects to filing the affidavit he has the alternative of going into court, where conviction may cost him $50 to $100. Many excellent devices are used to stimulate complete and prompt birth registration; 32 states send out to mothers a notification of filing of the child's birth; posters urging registrations are prominently displayed; and educational work is done in various ways by the Census and Children's Bureaus, and also by workers in the maternity and infancy field, and others. It is hoped that by 1930 every state will be in the birth-registration area.

Society Transactions

AMERICAN ASSOCIATION OF OBSTETRICIANS, GYNECOLOGISTS AND ABDOMINAL SURGEONS

THIRTY-EIGHTH ANNUAL MEETING

HOT SPRINGS, VA., SEPTEMBER 16, 17 AND 18, 1925

DR. ASA B. DAVIS, OF NEW YORK, PRESIDING

(Concluded from May)

In a Symposium on **Malignancy,** the following papers were read:

Sarcoma of the Stomach, by DR. GEO. F. CHANDLER, KINGSTON, N. Y. (See page 101.)

Metastasis in Breast Cancer, by DR. WM. A. COVENTRY, DULUTH, MINN. (See page 113.)

The Differentiation of Cancer Tissue, by DR. JAMES E. DAVIS, DETROIT, MICH. (See page 29.)

DISCUSSION

DR. HENRY SCHMITZ, CHICAGO, ILL.—To correctly evaluate the treatment, the cases should be grouped as we group the cases of carcinoma of the cervix, namely, Group 1, the clearly localized cases; Group 2, comprises cases in which there is doubt about localization to primary seat of invasion; Group 3, contains the cases with invasion of the contiguous tissues and organs without fixation, and Group 4, those with a fixation and extensive invasion. The same classification could be applied to the breast cases. The indications for the various methods of treatment are placed on this grouping.

In Group 1 the treatment indicated is radical excision, including the pectoralis muscles. There is no necessity of applying the x-ray or radium because all the cancer cells can be removed and the patient should remain well. In Group 2 there is a tendency of the carcinoma to spread, there is usually a very perceptible growth. Here x-ray should first be applied in a sufficient dose to cause occlusion of the lymphatic vessels and a degeneration of the cancer cells, so that they are for the time being stunned and rendered harmless. Operation then follows. In Group 3 we should primarily have recourse to radiation and if, after radiation, the carcinoma becomes movable and reduced in size, then we should add a radical excision. In Group 4 no form of treatment will do the patient any good.

It is, of course, natural that in the treatment of carcinoma of the breast we should pay particular attention to the mode of spread by metastases. We know that the spinal column, the hip bones and the heads of the femurs are the places most frequently involved, even after extensive primary treatment. Therefore x-ray pictures should be taken of every case of cancer of the breast before treatment. In recent correspondence I have had with Dr. Bloodgood about the matter we came

to the conclusion that if x-ray treatment can do these patients any good, the bones of the entire trunk should be included in the treatment to prevent the appearance of metastasis later on. If we wait until metastases occur, which are usually indicated by indefinite pains in the involved areas, x-ray treatment rarely will do the patient any good.

I have treated a great many carcinomata of the breast and recorded 180 cases which had been treated more than five years ago. They were divided into two classes, the primary and the recurrent carcinomas. Of all the cases of primary carcinomata, about 28 per cent have passed the five year period free from recurrence; of the recurrent cases 20 per cent have passed this period. I do not wish to say these cases may not eventually die from carcinoma, but they have passed the five year period well and free of the disease.

It has been stated that the so-called high voltage radiation will give better results than the low voltage, the essayist having used a 100 kilovolt current. It does not make any difference what kind of radiation one uses so long as the radiation is absorbed in the diseased tissue, and the 100 kilovolt will give as good results as the 200 kilovolt. We use both kinds of apparatus in Chicago and in carcinoma of the breast we decline to use the 200 kilovolt current because the results were very inferior to those obtained with the 100 kilovolt. The high voltage on account of deeper penetration will cause more damage to the lungs than the 100 kilovolt.

If I have any criticism to offer it is that the focus skin distance was too short and therefore the difference in intensity between the surface dose and the deep dose at 2 or 3 cm. was so great that the underlying cancer tissue received only a fraction of radiation, which in this instance was probably about 25 per cent. If a greater focus skin distance had been used—say 50 cm. or even 65 to 80 cm.—and a 100 kilovoltage, I believe the results from the x-ray radiation would have been better.

It was stated that some of these patients had received x-ray treatments at frequent intervals, as often as at twelve different times. Normal tissues will recover from the damage caused by x-rays after one application, and probably also after a second application. But if the application is continuously repeated we will cause a degeneration of healthy tissue, such as indurations and ulcers, which behave like a malignant disease. Therefore, we should make it a rule not to subject the patient to repeated x-ray treatments. If results are not obtained by one or two correctly applied radiations then the cancer is refractory and further applications are useless and dangerous.

The microscopic study by Dr. Davis is a very valuable contribution. If we apply his teaching method we will materially contribute to the correct diagnosis of cancer. The work done by Alter, Martzloff, Schottlaender and Broders in the study of the cell type of cervical carcinomata has greatly advanced our knowledge of the malignancy of cancer. Such typing should be made the foundation for treatment. A fat spindle cell, unripe carcinoma is much more malignant and resists treatment much more than the prickle cell or squamous cell cancer. The latter shows a higher percentage of five year healing after operation and also radiation than the fat spindle cell type.

DR. WM. W. BABCOCK, PHILADELPHIA, PA.—I speak with hesitation about a treatment we have used in apparently hopeless cases of malignancy during the past eighteen months. The principle is not new, is based upon the work of Dr. Hodenpyl and consists in injecting intravenously ascitic fluid from patients with cancer of the peritoneum. We have used very large injections—250 to 2,000 c.c.—and have found the fresh peritoneal fluid from other patients with carcinoma very well tolerated. Almost eighty injections have been given; the total number of patients being about forty. In two patients surprising improvement has followed the treatment.

A man found on an exploratory operation to have an apparently inoperable carcinoma of the stomach and considered hopeless, was given one injection and sent home to die. He soon gained 27 pounds, lost all symptoms and now has been back at work for a year and seems to be in good health.

The second case is that of a woman who was operated upon last year for advanced cancer of the uterus and then treated for recurrence by radium. The disease progressed, she developed a large fistula in the bladder and last Spring was finally confined to her bed under opiates. The condition was such that further treatment by radium was refused. After several injections, she showed surprising improvement both locally and generally.

Recently, she reported at the office, having the fistula but with little induration and no odor or bleeding.

The other patients treated have for the most part died. The fluids have been from various types of carcinoma involving the peritoneum with ascites. Here is a method of giving richly albuminous fluids in large amounts to replenish the tissues of the debilitated patients with carcinoma. To avoid reaction we have found blood and fluid typing less important than the use of fresh ascitic fluid.

DR. WM. SEAMAN BAINBRIDGE, NEW YORK CITY.—You may recall a report, previously made, of a series of cases of malignancy (a large number of which were in animals and a lesser number in humans) where hypodermic and intravenous injections of fluid were administered. There were about two dozen, not counting about twenty-five controls, in which we used hypodermics of saline, albumin, and various other fluids. As is true in many cases of advanced cancer, which may get better and then worse, regardless of the type of treatment used, we had temporary improvement in many of these cases. In some instances, we used ascitic fluid, while in others we used quite different fluids, and about as many patients showed this temporary improvement under the injection of the one fluid as under the other. All of the cases, however, eventually died, the course of their disease being unaffected by the treatment. Our experience with the Hodenpyl serum and its usefulness has been published.

DR. MILES F. PORTER, FORT WAYNE, IND.—I should like to ask the author of the paper on sarcoma of the stomach to tell us what these patients died of who lived from two to seven years? I would like to ask also regarding the metastasis to the liver by way of the lymph glands. Sarcoma does not usually metastasize in that way. What is the explanation?

A word regarding radiation in the attempt to cure cancer. I can recall three individuals who have died as a result of fibrosis of the lungs consequent upon, in my humble opinion, the use of the x-ray in extensive doses in the attempt to prevent metastasis from a carcinoma of the breast.

I should like to ask also how the diagnosis of the cancer, cured temporarily at least by the injection of the peritoneal fluid, was made? I at one time reported five consecutive cases of cancer of the thyroid. This diagnosis was made in the laboratory and the cases were cured by subtotal thyroidectomy. The explanation is that the diagnosis was wrong.

DR. CHANDLER (closing).—I cannot answer Dr. Porter's question because in all the literature there is nothing I can find on the subject. I am watching this woman and if I live long enough I will know what causes her death eventually. I have had a number of my colleagues look over these cases and there seems to be nothing that states what the patients die of. All the pathologists say that the metastasis in carcinoma of the stomach is through the lymphatics into the liver. I cannot explain it.

THE NEW YORK OBSTETRICAL SOCIETY

MEETING OF FEBRUARY 9, 1926

THE PRESIDENT, DR. O. PAUL HUMPSTONE, IN THE CHAIR

DR. P. H. WILLIAMS reported a case of **Rupture of Uterus Through Previous Cesarean Scar.**

Mrs. M. M., was operated upon August 17, 1922 in my service at the Lincoln Hospital. A classical, high incision, cesarean section was done because of generally contracted pelvis, a large fetus, and a pedunculated subserous fibroid about 7 cm. in diameter attached to the anterior wall of the uterus.

The operation was uncomplicated and the fibroid was removed. The uterus was sutured with a row of chromic gut sutures, including peritoneum and muscle down to endometrium, after a second row including the muscle alone had been inserted and tied; and followed by a continuous Lembert suture of plain catgut, covering the uterine incision with peritoneum. The abdomen was sutured in layers.

She made an uneventful recovery, except that there was a slight infection in her abdominal wound, and a rise of temperature to 104° F. on the fourth day. She left the Hospital in twelve days, with a healthy baby.

The following winter her doctor informed me that she was pregnant a second time, and I advised him to keep close watch of her, and to send her to the hospital promptly at the onset of labor.

On June 2, 1923, the patient telephoned me that she had no pains, but had felt for a few days a soft swelling in her abdomen. I advised her to go immediately to the hospital, and on the following day found, upon examination, that the uterus contained a full-term fetus in R. S. A., the head in the upper right quadrant, the presenting breech not engaged, the cervix rigid, long and undilated. A cystic mass which disappeared upon firm pressure and became more evident upon uterine contraction appeared at the umbilicus, behind which could be felt a firm hard ring, especially between contractions.

The patient had had no pains, and there were no signs of the onset of labor. An immediate operation was decided upon.

Incision was made to the right of the former scar. Upon opening the abdomen a cystic mass filled with semitransparent fluid presented itself, giving the appearance of a thin-walled unilocular ovarian cyst, but on pressure some of the fluid disappeared revealing a fetal arm, forearm and hand in the cyst. There was no blood nor bloody fluid in the abdominal cavity. In handling, the cyst was ruptured, with the escape of amniotic fluid through the abdominal wound. The ring-like scar was incised above and below, a full-term fetus removed and a supravaginal hysterectomy performed.

The abdomen was sutured in the usual way, and the patient made an uneventful recovery.

Upon examination of the uterus, the edge of the hole showed no roughness, no granulating area, and no signs of hemorrhage, and the endometrium seemed continuous with the peritoneal covering of the organ. The rim was of cicatricial hardness and was much less elastic and compressible than the surrounding uterine muscle.

The points which I wish to emphasize are: (1) there must have been a separa-

tion in the uterine wall and a herniation of the amniotic membranes at least forty-eight hours before the patient's admission to the hospital, without any contractions of the uterus, except the normal Braxton-Hicks phenomena; (2) there was no blood in the peritoneal cavity, nor other signs of a sudden rupture; (3) the tumor was the only thing noticed by the patient, who never complained of any pains, such as signalize the onset of labor.

DISCUSSION

DR. A. B. DAVIS.—I recall that about twelve years ago a patient was admitted several days before the calculated full term for her second cesarean delivery. Upon examination a very large fluctuating mass, at first thought to be an ovarian cyst, was found. It was decided to deliver this case by section without waiting for the onset of labor. Upon opening the abdomen a full-term fetus was found floating in the amniotic sac, the mass which had been taken for the ovarian cyst. The uterus, containing the placenta and fetus, had ruptured and contracted well down toward the pelvic brim. There was no evidence of blood, and the membranes were adherent to the edges of the uterine wall where rupture through the old cesarean scar must have occurred months before. To all intents we were dealing with an abdominal pregnancy with the placenta lodged in the uterus. The placenta was manually extracted; the edges of the old cesarean wound were freshened, and the opening was closed in layers in the usual way. The patient made a good recovery.

DR. W. E. CALDWELL.—Several years ago Dr. Cragin did a cesarean section at Sloane. At a subsequent delivery Dr. Bailey induced labor at Bellevue. That baby died. The second time the patient's abdomen was opened very much the same condition that Dr. Williams and Dr. Ryder described was found—membranes bulging through the uterine wall. We delivered the baby, repaired the old scar, and did a subsequent cesarean on this woman. The following year after that she had another cesarean and we sterilized her.

DR. E. T. HULL.—A few years ago I did a cesarean section which was of particular interest to me, because I saw the uterus when it ruptured through the old scar. The patient had had a cesarean section before that and had run some temperature postpartum. Upon opening the abdomen there was noted a blue line which looked like a distended vein extending along the site of the old incision, and that apparently was made up entirely of peritoneum. As I introduced my hand to see if there was a rupture of the uterus the upper part of the thinned out membrane ruptured and the placenta prolapsed through the rupture. I enlarged the rupture through the thinned-out scar and delivered the patient. I then cut out the thinned-out edges and was able to get good approximation. I did not do a hysterectomy. The patient and baby made a good recovery.

DR. P. H. WILLIAMS (closing).—In reply to Dr. Ryder I would say that I took out the uterus because I was of the opinion that there was a fibroid there. In fact, she had a previous fibroid which had been removed, and I thought that possibly I was dealing with a fibroid uterus.

DR. HUGO EHRENFEST, of St. Louis, Mo., presented (by invitation) a paper entitled **The Normal and Pathologic Physiology of Pregnancy.** (For original article see page 58.)

DISCUSSION

DR. W. W. HERRICK.—I have for a number of years, been very much interested in the medical study of certain phases of pregnancy at the Sloane Hos-

pital. It is interesting that our observations have led to much the same conclusions that Dr. Ehrenfest has expressed tonight in his paper, which shows a combination of broad clinical vision and meticulous scholarship.

It seems to me that during our own time we have seen three different phases of development of medical problems in process. The first phase, the study of disease as related to anatomic-pathologic changes in organs; the second, the relation of disease to disturbance in function. Those two phases of study tend to lead us to the belief that a given disease is associated with one organ or one group of organs. The third phase of study is one which we are just entering, that in which we are led to believe that many diseases are not related to structural or even functional disturbances of isolated organs or groups of organs, but are in their inherent nature a disturbance of general organic equilibrium, of correlation between organs in which hormone effects and the nervous system have important parts. In accordance with this hypothesis certain diseases are disturbances of general equilibrium and not necessarily a functional or structural disarray of a single organ or group of organs. It seems to me that certain disturbances of pregnancy illustrate this in a superlative degree.

Particularly have I been interested in the study of the toxemias of pregnancy, not only because of their inherent importance, but also because they suggest the direction in which the solution of certain important medical problems may be carried out. It seems to me that the toxemias of pregnancy are not unit conditions; that we shall never solve that problem by seeking for an isolated toxin or for a disturbance in any given organ or group of related organs, but that we must solve the problem along broader lines. During the last six years' study with the help of Dr. Jean Corwin along the lines of a medical survey of each of the cases of toxemia, it has been impressed upon us that the majority of these women who show toxemia of pregnancy have some underlying disease. This underlying disease is most often manifested in the gastrointestinal tract, the endocrine system, or predominantly, in the cardiovascular-renal system. What is the proof of this? The proof of the relation of the pathology in these cases to the gastrointestinal tract rests largely upon clinical grounds. We know that women with faulty habits of eating, faulty bowel function, such definite pathology as intestinal adhesions and bands, very often have a functional upset during pregnancy.

The endocrine system is certainly disturbed in many of these women who show toxemia. From the first we were impressed with the frequency of the so-called pituitary type of woman in our toxic wards; the woman who was overweight, who had rather coarse skin, who had virilism in hair distribution, often with spaced incisor teeth, with heavy muscles and large hands and feet. Dr. Draper was asked to make anthropometric measurements of a large number of these women. He measured 117 of them and found that they corresponded in measurements with the so-called pituitary type, the type which is most prone to cardiovascular disease, characterized by arterial hypertension. Can it be possible that the pituitary gland is astray in these patients and that this is a fundamental fault in the etiology of hypertensive cardiovascular disease, as of toxemia of pregnancy?

As to cardiovascular-renal disease, we have found that a very large majority of these women, studied at the time of their toxemia in the antenatal and postnatal clinics (some cases we have observed for over six years), show changes in the cardiovascular-renal system in the way of arterial hypertension, of that instability of the cardiovascular system which precedes established hypertension, in sclerotic changes in the retinal vessels or in the larger peripheral vessels, in cardiac hypertrophy or in persistent albuminuria. I think I am not exaggerating when I say that at least 75 per cent of the women in the toxic wards, or of the

women who have been through those wards, show changes in the cardiovascular-renal system. I believe that the relation between hypertensive cardiovascular disease and many of the toxemias of pregnancy is a fundamental one, and that the etiology of this most important and common disease that we call hypertensive cardiovascular disease, can be found related to the development of the toxemia of pregnancy. I believe that, if the toxemia of pregnancy is a failure of adaptation of the woman to the strain of pregnancy, hypertensive cardiovascular disease is also a failure of adaptation. Perhaps these two conditions are on related and similar grounds. I believe that the solution of the problem of hypertensive cardiovascular disease may be found in a study of these toxemias of pregnancy.

We are about to publish the results of our study of these cases at the Sloane Hospital. At the present time I cannot give you detailed statistics, but our present impressions are in agreement with the views of Dr. Ehrenfest that the toxemias of pregnancy arise from a failure of adaptation. We believe that toxemia occurs, rather because the woman is a deficient being and has some fundamental pathology, than because she is pregnant. I believe that the solution of many medical problems lies along this line and that a careful study of the reactions of a woman during pregnancy will give a very accurate prognosis as to her future reactions to the strain of life itself. With this point of view I judge Dr. Ehrenfest to be in accord. I think as a revealer of the pathologic trend of a woman the study of the reaction to pregnancy is of the utmost importance to the medical man.

DR. R. T. FRANK.—The enormous amount of material that Dr. Ehrenfest presented to us in his striking and masterly review of this subject is almost bewildering. At the same time to the attentive listener there was a distinct and very evident chain which started at the beginning and carried through to the end.

The first thing was his emphasis on the general aspect of the patient, the habitus. That, of course, is laid down, you might say, at the time of the mother's impregnation, the parents that were selected, life during childhood, development during puberty. These are the first things that must be considered and which will have a striking effect upon her ability to be a successful mother.

The second thing is the emphasis laid upon the premenstrual phase of the woman, i.e., before impregnation has taken place. Each growing follicle has a definite effect upon the entire maternal organism and especially upon the genital tract and the mammary system. When ovulation takes place, the corpus luteum continues the process. In the human female the evidence accumulating shows that ovulation probably takes place in the middle of what, from the uterine indications, we consider the premenstrual phase, and that after ovulation takes place the corpus luteum continues this hyperplasia of the entire genital tract in order to prepare for the ovum.

We now, as the term I am going to mention indicates, have evidence which enables us to see in what an impregnation without a fetus really consists. For instance, in the bitch, if impregnation does not take place, for fully forty days a process of pseudopregnancy occurs. The bitch would be an excellent subject in which to study the hypophyseal and other endocrine changes which may occur without the fetus and, therefore, it lends itself well to analysis. If impregnation takes place, in the first place the corpus luteum contributes to the hyperplasia, and as soon as the mass of chorionic tissue is sufficient, the placenta continues the endocrine process, and brings it to a successful conclusion at the time of labor. Gustavson and myself have tried to emphasize this frequently forgotten fact by coining the term *gestational hormone*, meaning thereby the secretion of follicle, corpus luteum, and placenta.

Then quite distinctly we have to deal with the fetal requirements and the reaction, which Dr. Ehrenfest also emphasized, of the fetus upon the mother. Now this reaction apparently, if analyzed, will be found to involve the genital sphere, producing the stimulation of the corpus luteum. I think that the continuation of the corpus luteum is undoubtedly due to the presence of fetal products, whether ferments or hormones. In other words, Dr. Ehrenfest has given us a very excellent generalization, and the only thing, small in itself, with which I could take any issue is the importance which he ascribes to placental ferments. I think they are as yet entirely unproved, except as any organ may contain ferments. That they have any general effect upon the maternal organization is, I think, inconclusively shown.

DR. HAROLD BAILEY.—I have been interested in this subject for twenty years, because it so happens that a case of mine in 1906 was the first in which the urine chemistry was studied throughout the pregnancy. The patient had pernicious vomiting in the early part of pregnancy and eclampsia at the end. I became a firm believer in the theory that one group of organs was responsible, and I retained this belief until 1913, when my attention was directed more particularly toward the liver. Since Dr. Titus showed us, in 1920, that the liver picture could be largely wiped out by sugar injections, I have felt that we must search further for the origin of this condition.

I think that the fetal protein is the actual cause of the disturbance, and I cannot but feel that further study along this line is logical, because we find emboli of syncytium in all parts of the mother. Furthermore, we know that under certain treatment the mother's condition clears up and the pregnancy goes on, even after eclampsia. So it seems that the fundamental fault can hardly be in the endocrine system, or in the relations between organs, for such conditions would hardly clear up so readily.

DR. EHRENFEST (closing).—I am far from claiming originality for these ideas. They represent the sum total of impressions I have gained from watching the trend of thought in obstetric literature for many years. Dr. Herrick very clearly pointed out how, in general medicine, failure, first with merely pathologic investigations, and later with chemical research, has finally lead to the present attitude of looking at the sick patient as an individual reacting in his own peculiar way to a disease that has attacked him. In a similar manner also the obstetrician should look upon the physiologic or pathophysiologic phenomena of a pregnant woman and her specific reactions to pregnancy. It is the main purpose of my paper to demonstrate that these reactions in general are those observed as well in the premenstrual stage. The general biologic effect of a certain phase of cyclic ovarian function continues and is modified if pregnancy follows the rupture of the graafian follicle. This thought of a continuity of ovarian hormone effect has been well brought out by the remarks of Dr. Frank. He and his coworkers have convincingly proved that follicular, corpus luteum, and placental hormones represent a practically continuous chain of potent substances which determine woman's sexual development and life from puberty to menopause. In my belief, these generative or gestational hormones determine to a great extent whether or not the pregnant woman will adapt herself promptly or completely to the various demands made upon her by pregnancy, granted of course, that she is a constitutionally normal and healthy individual. If she has deficient organs, full adjustment may become impossible. The demands of pregnancy may cause further deterioration in already damaged organs or may reawaken old processes. I thoroughly agree with Dr. Herrick that the seeming direct causation of a disease by pregnancy as

a matter of fact most frequently represents only the exacerbation of a preexisting condition, as I have mentioned, e.g., in speaking of pyelitis.

Dr. Bailey might find in reexamination of the patient he mentioned, that she is now suffering from a true nephritis. By insisting that some toxic substance passes from fetus to mother, he does not contradict my views as markedly as he thinks. I also admit that various substances pass from fetus to mother, but I maintain that they are not *per se* toxic, but become toxic only when the mother for some reason is not able to take care of them properly. The mother in this case is not able to adjust herself adequately to certain demands, though the demand itself is only physiologic. And I may emphasize once more, failure upon the part of the mother to adapt herself promptly or completely to the demands of pregnancy does not necessarily result in the accumulation of toxic substances in her blood, though all too readily the clinical picture is termed a toxemia.

DR. I. C. RUBIN presented a paper entitled **Sterility Associated with Habitual Amenorrhea Relieved by Roentgen Therapy.** (For original article see page 76.)

DISCUSSION

DR. J. A. CORSCADEN.—My experience with curing sterility by x-ray has been limited to two cases, without amenorrhea, and I think that probably makes a great difference. They were both without result. They were undertaken merely in the excitement of reading of the work when it was first done. We did not persist in it, because we were very much more occupied in attempting to produce the opposite effect, namely, sterilization in women with uterine hemorrhage and myomata. We were further inhibited by these same questions which Dr. Rubin raised as to the fundamental causes of the sterility, the knowledge that pituitary disease very often plays a rôle in sterility, the knowledge that thyroid therapy often cures the condition, etc., further, that amenorrhea was not entirely a measure, or at least an indicator, of sterility. In that connection I might cite a case that we found recently in the clinic, of a woman who has never menstruated, but who has had five normal children and four miscarriages, whose mother had the same history (I forget how many children she had), whose sister menstruates regularly and has never been pregnant—rather a peculiar combination of circumstances.

Secondly, we were held back by a wholesome respect for the x-ray, with its dangers seen and unseen. After one has worked with it personally one always hesitates to apply it without a very compelling reason. I must say, however, that our real reason has been that we were occupied with its other usages. The fear of attempting a new thing because it might do some harm, I think, is not always entirely worthy. If our ancestors hadn't taken some chances, I suppose we would still be hanging to the trees by our tails.

The danger to the fetus is, so far, based upon experimental evidence. There is some evidence that the lower orders are more susceptible to these germ plasm changes than the higher orders; that is, we call ourselves higher. For that reason I think that the presentation of such a fact, namely, that we have nine out of twelve cases apparently relieved, is reassuring. I do not know of any one who needs more help than one of these women who is told that her sex organs are normal, the so-called primary sterility, or nearly normal, and that the examiner can find no reason why she should not become pregnant. She will accept more or less the sterility following hysterectomy, or that due to tumor, inflammation, or some obvious thing, but the state of mind of the woman who thinks she has perfectly normal

organs and is kept sterile by some unknown force is most distressing, and I congratulate Dr. Rubin upon his results.

DR. HARVEY B. MATTHEWS.—These results bear out what we have believed from a recent comparative study made of rabbits and of human ovaries after irradiation. From this study, I have persistently maintained that a therapeutic dose of irradiation, be it x-ray or radium, would not be injurious to pregnancy, and, furthermore, that there was no reason to believe that the offspring would possess any anatomic abnormality.

Dr. Rubin spoke about the irradiation of the corpus luteum, saying that it was destroyed early. In our experiments upon the rabbit we found that the corpus luteum was the very last element to be destroyed following irradiation. The ripe follicles went first, the primordial follicles next, the germinal epithelium next; while the corpus luteum was the most resistant and, therefore, the last to be destroyed. This series of facts was borne out in the case of a woman that we studied, who had had a full carcinoma dose of 4,000 mg. hr. of radium, with hysterectomy four months later. We studied the ovaries. She had persistent corpora lutea with absolutely no other part of the ovary recognizable, no follicles of any kind and no germinal epithelium.

This study bears out the fact that there is no reason why a woman cannot become pregnant after a therapeutic dose of irradiation. Just how stimulation of the ovary takes place in these cases of amenorrhea and sterility, I am, of course, not prepared to say. There are evidently some changes within the follicle, and I would imagine that the primordial follicles that are not destroyed by the irradiation develop in a normal manner, and that there are perhaps, some inherent changes in the ovarian stroma, or in the germinal epithelium, or perhaps in the persistent corpora lutea, if there were any. These "runners-up," are in a healthier condition following therapeutic "doses" of irradiation. Otherwise, I do not offer any explanation.

Of course, irradiation after conception has taken place is an entirely different matter. We know from many case reports in the French, German, Russian and Scandinavian literature that there are anomalies of various organs, particularly of the central nervous system, due to radiation after impregnation has taken place.

DR. IRA I. KAPLAN.—The idea of stimulating the ovary is based upon the assumption that if we stimulate any biologic tissue in the body we create a response to this stimulation. As a response to any inflammatory reaction, the vascular supply, the flow of the blood cells, mostly the leucocytes, and, therefore, perhaps, the tension in the ovarian follicles is increased. This tension causes an explosion, as it were, or a rupture, which brings forth the new ovum which travels down and later becomes impregnated, or brings on menstruation, first, and then probably impregnation.

We must assume, then, that a certain dosage will cause this without stimulating the formation of fibroblasts, which create scar tissue formation or fibrous tissue, and, therefore, after much experimentation, it has been assumed that this dose is probably equivalent to approximately one-third the castration dose on the ovary. This is a little different than the third of the erythema dose, for if we give a dose of 100 per cent on the skin, according to the type of apparatus used, a certain amount of the dosage is absorbed by the tissue intervening between the surface of the skin and the ovary which you are attempting to radiate. Therefore, you must calculate the dosage so that the dose on the ovary is approximately 10 per cent. The variance is between 10 and 12 per cent in the usual run of cases. I have calculated that dose in my method of treatment. I give approxi-

mately 4 per cent from the front on the ovary and 6 per cent from the rear. The reason is that radiating through the abdominal wall there is much more absorption on account of the intervening layers of intestinal tissue, etc., and the dosage is lessened; from the back, while there is a great deal of absorption from the bony structures—and we give a larger dose from the back—an increased dose on the ovaries, due to the increased scattered radiation from the bony structures is obtained. This bony absorption is explained in the x-ray photographic plate; the bone structure absorbs a great deal of radiation and gives a shadow. Also, the bones give off a secondary radiation, and by actual ionization experiments it is found that the ray reaching the ovary in the back is of greater intensity than the one from the front; consequently about 6 per cent on the ovary from the posterior surface and 4 per cent from the anterior surface should be given. Thus there is 10 per cent on the ovary. Usually that is sufficient for bringing on menstruation. If it does not bring on the menstruation after a period of two to three weeks, the treatment is repeated in about four weeks from the time of the initial treatment. I never repeat after the second treatment, because then castration is certain.

BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF FEBRUARY 5, 1926

Dr. Ralph M. Beach reported **Two Cases of Pregnancy Complicated by Fibroids.**

Case 1.—Mrs. C., twenty-eight years old, a primigravida, married three months, was first seen by me Aug. 25, 1922. She had menstruated first at the age of fourteen, five to six week type, flowing six days, with comenstrual pain for half a day. Her last menstruation was May 8, 1922. General physical examination showed the heart, lungs, blood pressure, etc., to be normal. Abdominal examination revealed a median hypogastric tumor extending to the umbilicus. This mass was soft and felt like a pregnant uterus, though the amenorrhea was of only three and a half months' duration. There were no fetal heart movements. The culdesac contained a hard tumor mass, about the size of a tangerine.

Diagnosis: Subperitoneal fibroid complicating pregnancy. Gentle manipulation, in the knee-chest position, failed to dislodge the tumor, and the patient was advised to assume the knee-chest position twice daily, and report in three weeks.

This patient was seen at three week intervals; life was felt at four and a half months. At the fifth month she began to have rather severe backache and lower abdominal pains simulating labor. She was in the hospital for a week at this time and required morphine at intervals to control the pain. The tumor was still in the culdesac and could not be dislodged. There was no constipation. At six and a half months the above symptoms were repeated and the patient was again kept in the hospital for a week. From this time on the patient was more or less uncomfortable, requiring rest in bed and codeine at frequent intervals. By the end of the seventh month she was beginning to have steady pains in the left groin and in the middle of the back with some edema of the left leg. Vaginal examination revealed the tumor somewhat higher in the pelvis and toward the left posterior quadrant. The tumor itself did not seem to be very tender at any time and the symptoms seemed to be due rather to peritoneal irritation and nature's efforts to get the mass out of the pelvis.

All of the above symptoms continued until eight and a quarter months when they suddenly disappeared. Vaginal examination at this time revealed the culdesac free of any mass and the head dipping well into the brim.

The labor occurred three weeks later in the Israel Zion Hospital, the baby being delivered by low forceps, due to secondary uterine inertia.

This case gave us no trouble during the puerperium and at the end of six weeks the patient was symptom free. A small fibroid could be felt springing from the posterior uterine wall, apparently just above the internal os.

CASE 2.—Mrs. R., thirty-two years old, a primigravida, was first seen by me Oct. 7, 1925. Her mother and one of her two sisters had uterine fibroids. She had been married five years and had practiced contraception until recently. Menstruation began at sixteen, regular four-week type, moderate flow lasting three days, with slight pain at times. Her last menstruation was July 29. Abdominal examination revealed a large tumor mass in the hypogastrium extending 17 cm. above the pubes. It was slightly irregular in outline, hard, not tender and appeared to be a fibroid uterus. Vaginal examination showed anteriorly a softened portion of the uterus evidently that containing the embryo, and posteriorly, in the culdesac, a hard tumor mass about the size of a tangerine.

An attempt was made, in the knee-chest position, to displace this subperitoneal fibroid from the pelvis but without success.

The subjective symptoms were, backache, constipation, and hemorrhoids.

About four weeks later, the patient had an attack of severe pain referred mainly to the back, but also to the groins. These pains were more or less constant, did not resemble labor pains, and there was no bleeding. The pelvic fibroid was rather tender on vaginal examination, and the symptoms seemed to point to an effort on the part of nature to pull this mass out of the pelvis. With rest in bed and codeine, the symptoms disappeared in three days. The fundus uteri at this time was 22 cm. above the pubes, about the size of a seven months' pregnancy. Two weeks later, on Nov. 22, the patient again began to suffer from severe backache and pelvic pain, and did not respond to treatment. The entire abdominal mass was tender and the pelvic mass much more so than at any previous time.

The patient was sent to the Methodist Episcopal Hospital the next day for observation.

An enema was followed by severe pains in abdomen and back. Blood count: hemoglobin, 70 per cent; red cells, 4,000,000; white cells, 19,000 and polynuclears, 89 per cent. In view of the continuance of the symptoms, pain being relieved only by morphine, a laparotomy was decided upon.

Median hypogastric incision showed the lower portion of the uterus containing the embryo (about three and a half months' size), while the main portion of the uterus above was occupied by one large interstitial fibroid, extending to the diaphragm. There was also a pedunculated subperitoneal fibroid the size of a lemon springing from the right anterior uterine wall, twisted around the right broad ligament and incarcerated in the culdesac. This created a marked dextrotorsion of the entire uterus through 90°, the left adnexa lying almost in the midline. The pedunculated tumor was removed by ligation of the pedicle with the idea of preserving the uterus. Proximity of this tumor to the right broad ligament vessels caused uncontrollable bleeding. The size of the other tumor seemed to preclude the possibility of the patient going to term, and a supracervical hysterectomy, and bilateral salpingo-oophorectomy was performed, with peritonealization of the stump.

The postoperative course was uneventful.

DISCUSSION

DR. A. C. BECK.—In our experience with pregnancy associated with fibroid of the uterus the conservative plan, such as was followed in these instances, has been pursued. Usually as the cervix dilates, the obstructing fibroid is pulled out of the pelvis and so out of the way for a spontaneous delivery. In regard to the case operated, I feel that the Doctor did the only logical operation permissable.

DR. A. M. JUDD.—One cannot determine the exact nature or extent of an operative procedure until the abdomen is open. At times these fibroids are found adherent to the rectum, and an extensive operation may be necessary to free them.

DR. C. A. GORDON.—I find it hard to make a general statement in regard to the treatment of fibroids complicating pregnancy. In general I would say that a fibroid in the lower uterine segment has a very good chance of being pulled out of the pelvis as labor progresses. I feel that each case must be watched and no definite course decided upon until the course of labor points the way.

DR. P. B. BLAND, of Philadelphia, read, by invitation, a paper entitled, **The Conservative Treatment of Uncomplicated Retrodisplacement of the Uterus.** (See page 89.)

DISCUSSION

DR. F. C. HOLDEN.—In Bellevue Hospital there were 11,459 admissions to the Gynecologic Department with an operative incidence of 22 per cent. I am not in entire accord with Dr. Bland in respect to retrodisplacements. I like to think of them, first as congenital or acquired and second, to note the relation of the fundus to the cervix. To determine whether or not a retrodisplacement is causing symptoms I think it well to replace the uterus, if that can be done, and then hold it in place with a pessary. If the symptoms complained of are relieved by this procedure, it is fair to assume that the retrodisplacement was the cause of the symptoms complained of. Every case needs individualization.

DR. J. O. POLAK.—It is refreshing to note that posture, pessary, and tampon are at last recognized as definite measures of conserving the pelvis. There is no question that the uncomplicated congenital retroversion produces no symptoms, provided the woman does not get infected, does not get married or does not become pregnant. If any of these things come to pass we may find a definite train of symptoms, because of the definite tendency to circulatory stasis in the broad ligaments. I believe that Dr. Holden's point concerning acquired versus congenital retrodisplacement is well taken. The pity is that the younger men do not appreciate what can be done by patience and persistence in the use of the pessary, posture, and tampon in these cases. Retroversion, the result of infection, childbirth or interrupted coitus, causes a good deal of disturbance. I agree with Dr. Bland that the so-called anteflexion is part of the symptom-complex, endocrine imbalance.

DR. H. M. MILLS.—I am glad for this note of conservatism as the present-day teaching tends to make the young doctor regard a retrodisplacement in the same light as he would an acute appendix; i.e., as an immediate cause for surgery. I agree with Dr. Polak that the cause of many of the symptoms produced by retrodisplacements is circulatory stasis.

DR. G. GIBSON.—Embryology will help to explain the uncomplicated retroversion, for in the fetus and even in early adolescence the uterus is high in the pelvis

and back in the pelvis, and it is only at puberty that it assumes the so-called normal position and at this time, in many women it does not come forward. After the menopause, in many women, the uterus assumes a retroverted position.

DR. C. A. GORDON.—I think the crux of the situation is the level of the cervix in the pelvic cavity. If that is approximately normal the retroversion needs no treatment. I disagree with Dr. Howard Kelly when he says that "the pessary is obsolete and almost of no value."

NEW ORLEANS GYNECOLOGICAL AND OBSTETRICAL SOCIETY

MEETING OF FEBRUARY 18, 1926

DR. PETER GRAFFAGNINO read a paper entitled **Air Insufflation of the Tubes.** (See page 98.)

DISCUSSION

DR. A. H. GLADDEN JR.—You have warned us several times against using this method in cardiac patients; what indication would there ever be for subjecting such women to it? As a usual thing we are not desirous of having such patients become pregnant. Is auscultation not a satisfactory method of determining the patency of the tubes when attempting to insufflate them? Also how many have you opened up after this method had been used?

DR. JOHN F. DICKS.—Have you had any bad results after using this method, and particularly, could you trace any infections to it?

DR. P. T. TALBOT.—Is there any method by which the patulous or nonpatulous side can be identified? Have you had any complications, such as a resulting salpingitis or the spread of some already existing infection? Do you consider it possible that a sterile tube might be infected by air whose sterility has not been checked up? That is, do you consider air a possible infectious medium?

DR. P. W. CARTER.—I have never done air insufflation of the tubes myself, but I have read considerably on the subject and am very much interested in it. Certain points came to my mind as I heard Dr. Graffagnino's paper and I should like them cleared up. Has it been necessary to put any of the patients under anesthesia to dilate the cervix? More than once, in attempting to diagnose a suspected case of stenosis in my office, I have been unable to pass even a sound through the cervix, and I am wondering how, in such instances, it would be possible to pass a cannula, which is definitely larger. Like Dr. Talbot, I am interested in knowing whether it is possible to determine which side is patulous. I should also like to know whether you have any idea of the number of cases, previously sterile, who have conceived since insufflation was done. I refer particularly to those patients whose tubes were occluded at the time of the first insufflation, but in whom the agglutination cleared up after repeated treatments. If not, do you consider that agglutination has taken place again? I realize, of course, that in certain patients pregnancy never takes place, even though the husband has been eliminated as a factor and the wife's condition presents no obvious bar to conception, but I am interested to know whether in your series of cases any other factor might explain the continued sterility. In the patients subjected to laparotomy after this treatment have your operative findings coincided with the findings demonstrated by insufflation?

DR. L. A. LEDOUX.—Did the cases which continued sterile after the test have another check made on their condition?

DR. HENRY MACHECA.—In connection with the general subject of sterility I should like to add that in the last few months I have seen three patients become pregnant after resection of the tubes with burial of the ends in the broad ligament. One miscarried at four months, one went to term, and one is now three and one half months' pregnant. I have also seen several cases, about four, who were apparently sterile, conceive after an irritating condition about the cervix had been cleared up. Whether I am right in ascribing the conception to the clearing up of the condition I do not know, but it does appear to be cause and effect; the patients were definitely sterile, the cervical condition was treated, and conception followed. At any rate, it suggests that merely clearing out occluded tubes might not accomplish the desired result alone, and that chronic cervical infections should be cleared up in conjunction with insufflation of the tubes if we hope to secure the best results in this unsatisfactory and baffling condition.

DR. P. GRAFFAGNINO (closing).—Replying to Dr. Gladden's question about cardiac cases, I would emphasize that this method has, for the most part, a diagnostic value, and that frequently its purpose is to prove the existence of pelvic disease as well as to make conception possible. Cardiac patients, of course, are not exempt from pelvic infections, and it was against the employment of this diagnostic method in the presence of organic lesions that I wished to warn you. Auscultation is a possible method, but not a very satisfactory one. I might say that when we began this work we insufflated every preoperative case of chronic salpingitis and checked our operative findings against the insufflation findings as a routine measure. The results agreed so uniformly that we no longer do this as a routine. Replying to Dr. Dicks, we have had no bad results at all which could be attributed to the employment of this method. Replying to Dr. Talbot, the only way in which the offending and patulous sides can be identified is that suggested by Kennedy in 1922, so far as I know. He injected sodium bromide into the tubes under pressure, and then took a skiagraph immediately afterwards, thus showing the existence and location of the occlusion. As I said to Dr. Dicks, we could trace no bad results to this method, and certainly we had no resulting salpingitis or other type of infection. Two of the patients fainted, and one woman complained bitterly for a few days of pain and discomfort, especially when standing; in her case I am inclined to think we used too much air. I do not regard air as an infectious medium. As I have emphasized already, the strictest asepsis is observed throughout. The patient is prepared as carefully as if for delivery or operation, and every instrument is sterilized. Replying to Dr. Carter we have had no special difficulty in introducing the cannula. Occasionally a small Jolie dilator was used to open the cervix gradually, but anesthesia has never been necessary. We have encountered no instances of true stenosis. I am sorry to say that we have been unable in most instances to check up our findings, in order to establish the fact of continued patency of the tubes. We urge the patients to return to the clinic for repeated examination and treatment, but as practically all of this work has been done at Charity Hospital, you will understand the failure of our follow-up records. I cannot, of course, attempt to explain why those patients do not conceive whose pelvic condition is apparently normal, whose tubes have been rendered patulous, and where the husband has been eliminated. Such cases are on record everywhere, and they furnish one of the unsolved problems of our specialty. As I have already said, our operative findings confirmed our insufflation findings practically uniformly when we were investigating that phase of the subject.

DR. P. T. TALBOT presented a case of **Intracranial Injury in a Newborn Child.**

Mrs. B., white female, was admitted to Hotel Dieu in labor the morning of August 31, 1925, labor being terminated that afternoon about 4 o'clock. It was uneventful in every way, except for the administration of two small doses of pituitrin during the afternoon to stimulate rather sluggish pains. No instruments were used and no lacerations occurred. The puerperium was equally uneventful. The child was a male, weight 8 pounds, 4 oz., and was born markedly cyanosed. The heart was definitely beating, but respiration was established only after considerable difficulty by means of oxygen and the classical methods of artifical respiration. The child never cried satisfactorily, and in spite of every effort the respiration continued irregular, at times becoming quite stertorous, so that oxygen was given as indicated for several hours. The excretions were normal, and by the morning of the following day his condition seemed fairly good. That afternoon, however, muscular contractions began, being most marked in the right arm, the left leg, and the face, with the interval between them about fifteen minutes. Dr. Signorelli was at once asked to see the baby in consultation, and the future treatment was entirely under his direction. Iodides were given, together with horse serum, and an ice cap was applied to the head. Several hours later true convulsions developed, lasting from a few seconds to several minutes, and most manifest in the arms and legs, particularly the left arm. There was also considerable squinting of the eyelids. Respiration was improved, however, and the child nourished well. September 2 convulsions occurred at irregular intervals, the baby sleeping between the paroxysms; September 3 only occasional muscular twitchings were present, and on the following day these also ceased. September 5, because of a decided gastro-intestinal disturbance which prevented nourishment by mouth, 50 c.c. of normal saline solution was administered by hypodermoclysis. September 6 the condition was worse, temperature 104, pulse rapid and weak. Stimulants were given throughout that day and night and were continued the following day. Hypodermoclysis was given as indicated for another week. At that time a slow but definite improvement began, which continued until September 20, three weeks after delivery, when the child was discharged. I have seen the child at intervals since, though he is, of course, under the care of a pediatrician, and in a general way I may say that I am far from satisfied with his condition. Dr. Signorelli believes that his progress has been good and that he will show no mental or physical effects from his stormy infancy, but I am not so optimistic. To me, the child has a rather blank expression, is decidedly not as observant as a baby of his age should be, and does not cry lustily.

I have presented this case, not because it is particularly unusual in itself, but to provoke some discussion of this important subject. I have read the literature rather widely, and I have been impressed, as I have done so, by several striking points. One of these is the relative frequency of the occurrence of spastic paralyses of various sorts, as well as the many mental abnormalities of later life which can be attributed to birth injuries, although many of them passed unnoticed at the time because there were no tangible manifestations to call attention to them. What steps are we to take to prevent such injuries, concerning the ultimate outcome of which we can only conjecture? They may pass unnoticed at birth, as I have said, and they may follow any sort of delivery. Are they unavoidable in most instances, or are they due to poor obstetrics? Again, when is operative interference indicated when the injury is immediately evident? In this particular case operation was considered, but the pediatrician felt that progress was satisfactory without it. I was rather interested, however, in another case delivered at the same time as this one, by forceps, which resulted in very obvious symptoms of intracranial

hemorrhage. Craniotomy was done; several blood clots removed, and the child made a perfect recovery. The location of the hemorrhage was the right temporal lobe. That baby, to my mind, is now perfectly normal in every respect, and I consider his condition far better than that of the child in the case I have reported.

This is, of course, an informal summary of certain points suggested to me by this particular case. The literature on the subject is voluminous and well worth an intensive review. I shall be interested to have the opinion of the Society on the procedure adopted in this instance.

DR. JOHN F. DICKS.—Within the last year and a half I have seen three cases of intracranial hemorrhage; one following normal labor, one following a midforceps delivery, and one, last week, following a face presentation. All of the children recovered. I believe there is undoubtedly in some cases a connection between intracranial hemorrhage and hemorrhagic disease of the newborn, and I believe also that Ehrenfest is right when he says that most intracanial hemorrhages of clinical importance are of the tentorial type. To my mind operative procedures are practically never justified because of the very high mortality, and because of the fact that spinal puncture is a simpler procedure and gives a higher percentage of cures. In all three of the cases I have mentioned the symptoms were the same. For the first seventy-two hours everything seemed normal, although afterwards it was recalled that in each case the babies had slept practically all the time. Then the breast was refused, they began to vomit, the temperature shot up to 103 or higher, convulsive tremors began, finally true convulsions. The treatment in all cases was the same; I might say that Dr. Delahoussaye handled one, Dr. Bloom the others. The convulsions were controlled by chloral, spinal puncture was done and repeated as indicated, and fluids were forced in every possible way. The children a year and a half and six months old are apparently normal in every respect, and the child born last week also seems normal, but as Dr. Talbot has emphasized, the ultimate fate of the child is what is most important in these cases, and as to that we can make no prognosis. In none of these cases was there any instance of hemorrhagic disease, and to my mind they are all illustrations of the true tentorial type of injury, in which craniotomy could do no good. An interesting consideration in this important subject is that we cannot foretell when such injuries will occur, as every type of labor seems at some time or other to result in them. One of my cases, as I have said, was a labor that was normal in every respect, and yet brain injury followed. On the other hand, I recently saw three physicians deliver a case with forceps, and that child was born without evidence of hemorrhage. The midforceps case to which I have referred presented only moderate difficulty, and the child was born without evidence of scarring or pressure. The face presentation is the most interesting case. When I first examined the mother she was 3 fingers dilated, and was having relatively mild pains. Suddenly, just after the examination, terrific pains began, and when I examined her again, not more than five minutes later, the face had come down on the perineum and was perfectly black. I did an immediate episiotomy and lifted the head gently over the perineum with forceps, the child breathed readily, and after some little effort began to cry. After seventy-two hours the symptoms I have outlined began, the temperature went to 106, and death was apparently imminent. By heroic measures, however, the trouble was checked, at least temporarily, and at present the child is apparently normal. Blood transfusion sometimes helps these babies, and in my second case this was done directly under the skin, the theory being that the coagulation time is improved by this procedure and the bleeding checked. Horse serum is sometimes efficacious for the same reason. In all these cases the coagulation time was within normal limits, and there was no external and visible evidence of trauma.

DR. P. W. CARTER.—A recent issue of the *Journal of the American Medical Association* contained a very interesting article detailing the results of spinal puncture on some 300 newborn children, the series including both those with and those without symptoms. In each instance the puncture was done within twelve hours after delivery. The findings in a very large percentage—I do not recall the exact figures—varied all the way from a mere yellowish discoloration of the fluid to bright red blood. Two babies, as I recall, died as a result of the original injuries. All the hemorrhagic diseases of the newborn, whether of the essential type or due to some brain injury, are akin, and frequently, as you know, it is not possible to differentiate them. Was a spinal puncture done in Dr. Talbot's case? And what was the coagulation time? I think the general opinion today is that spinal puncture gives considerably better results than operative measures; it may be repeated as often as indicated, that is, until the discoloration of the fluid disappears and convulsions cease. In this connection I should like to report a rather interesting case of hemophilia under my care a few months ago. I first saw the mother when she was six months pregnant, at which time her coagulation time was thirteen and one half minutes. By treatment it was reduced to three and one half and her delivery was without incident. The child's blood was examined at birth, the coagulation time being three minutes. That afternoon, when I examined him again, I found blood issuing from the cord; this was definitely not due to the tie. The cord was tied twice, as is my invariable custom, with separate ligatures, and this hemorrhage, which was of a very mild character, was issuing between the tie and the abdomen. The condition rapidly cleared up, but I refused to circumcise the child, in spite of the continued low coagulation time, because of this very definite diapedesis. Another somewhat similar instance might be mentioned also. The mother's first pregnancy terminated in an induced labor at eight months for eclampsia. Two years later she had an entirely normal, full-term pregnancy. Twenty-four hours after birth the child began to vomit blood, and also to pass blood by rectum. Three days of treatment by horse serum cleared up the condition and to date there has been no recurrence. The origin of these conditions is unknown, but there is certainly some underlying relationship between the hemophilias, the internal hemorrhages and the cerebral hemorrhages of the newborn. The most important point to be emphasized in such a discussion is the necessity of watching the children. Faint twitchings and slight tremors are too often disregarded until it is too late. A spinal puncture in any suspicious case does no harm, and may be the means of both diagnosing and clearing up a condition which, if untreated, will jeopardize the child's whole future. The good results of this treatment can easily be explained: by the reduction of the pressure, the exudate is either absorbed or drawn off before it clots, and further trouble is thus avoided.

DR. L. A. LEDOUX.—In spite of the immense literature on the subject of hemorrhage in the newborn, it is evident that as yet we have only scratched the surface of this immense field. Several points are suggested by this particular case. I am wondering, for one thing, whether the two doses of pituitrin, no matter how small, might not have been responsible for the injury. The labor was normal in every respect, the duration was average, and no instruments were used, and, unless the pituitrin was responsible for an increased overlapping of the cranial bones, there is no explanation for the injury which occurred. In my service we have been doing spinal punctures for the last three years in every case in which we suspected brain injury, both for the diagnostic and the therapeutic effect. Difficulty in establishing normal respiration after delivery should make us suspicious of these injuries, and vomiting or inability and lack of desire to nourish is another important diagnostic point. In every single instance in which we did a spinal puncture and removed blood stained fluid, whether under pressure or not, there was a definite improvement. If Dr. Talbot, in comparing a case handled by operative meas-

ures with his own, is referring to the same case I have in mind, I might say that in that instance craniotomy was done five days after delivery, when the child was practically moribund, and for my own part I consider the fortunate outcome a mere piece of good luck. Craniotomy in cerebral hemorrhage in the newborn has such an appalling mortality that few of us would care to advocate its routine performance. I think I may safely say that the physician who handled this particular case has learned since that spinal puncture is good obstetrics and good pediatrics, and that he is likely to handle future cases by the simpler method. The solution of the whole problem, as Dr. Carter has emphasized, lies in more careful watching of the newborn babies, so that slight symptoms shall not be disregarded.

DR. P. GRAFFAGNINO.—Spinal puncture has a definite therapeutic value in intracranial hemorrhage. Of late we have used spinal analgesia frequently in our operative work, and careful checking has shown a considerable drop in blood pressure within fifteen or twenty minutes after puncture was done. I recall at least one instance in which a systolic pressure of nearly 300 dropped to around 70 in a short time with no apparent effect on pulse or respiration. Repeated puncture in hemorrhage of the newborn, by reducing the blood pressure, enables coagulation to take place sooner, and this seems to me one of the principal reasons for advocating its routine performance in such cases.

NEW YORK ACADEMY OF MEDICINE, SECTION ON OBSTETRICS AND GYNECOLOGY

STATED MEETING, HELD NOVEMBER 24, 1925

DR. EDWIN W. HOLLADAY IN THE CHAIR

DR. RALPH A. HURD reported two cases of **Ovarian Cysts Removed During Pregnancy Without Its Interruption.**

CASE 1. Age twenty, pregnant for the second time, came into the outpatient department of the Woman's Hospital during her sixteenth week complaining of sharp abdominal pain and general prostration. A mass the size of a large grapefruit and slightly tender was found occupying the umbilical region, while pelvic examination confirmed the presence of a normal intrauterine pregnancy. The mass was very freely movable and could be pushed upwards and outwards into either hypochondriac region. Dr. Dougal Bissell performed an abdominal section two days later. The mass proved to be a pedunculated dermoid of the left ovary which had become twisted at its pedicle almost to the point of strangulation. The entire appendage on that side, together with the tumor, was removed and the right normal ovary allowed to remain *in situ*. In this case it is assumed that the lutein cells were present in the removed diseased ovary as the corpus luteum of pregnancy could scarcely have been overlooked in the small normal ovary at sixteen weeks, when it would occupy a third or more of the total size of the organ.

Here, then, is a case of pregnancy uninterrupted after total removal of one ovary containing a large dermoid and, in all probability, a true corpus luteum body, this opinion being based on the absence of the latter in the normal ovary which remained.

CASE 2. A primigravida of twenty-three, who was first seen in the twelfth week. History negative except for a variable degree of dysmenorrhea, and she had never before had a pelvic examination. Her last menstruation was normal, had occurred on November 3rd. On January 20th she went to her physician for examination and

advice concerning her suspected pregnancy and was referred to me for obstetrical care.

Examination showed a somewhat soft uterus which gave the impression of an early pregnancy, but in addition to this there was a globular, elastic mass, quite insensitive, which filled the entire pelvis and extended upwards into the abdomen almost to the level of the umbilicus. A diagnosis of ovarian cyst was made.

On account of the possibility of complications arising later in pregnancy, laparotomy was performed. The right ovary was the seat of an irregularly spheroid cyst, somewhat constricted at its central portion, which had attained the size of the head of a newborn and which had so invaded and distorted the organ as to render the normal ovarian tissue no longer recognizable. A smaller tumor of similar type, the size of a hen's egg, was found arising from the left ovary, while both tubes appeared quite normal, and a pregnant uterus, corresponding in size to the duration of her amenorrhea, occupied the anterior part of the pelvic cavity. Oophorectomy, together with resection of the cyst, was performed on the right side and the smaller tumor excised from the left ovary, leaving a crescentic rim of normal tissue on one side as the patient's only remaining ovarian substance. In this, again, there was definitely no corpus luteum substance so far as careful inspection was able to demonstrate.

The pathologist reported from both sides the various elements which characterize dermoid cysts of the ovary, including formation of bone and teeth. The sections taken did not show lutein cells, although they are assumed to have been present somewhere in the tumor mass.

The patient made an uneventful operative recovery and continued with her pregnancy quite normally. She went into labor a few days before her expected date of confinement and was delivered of a normal male child, there being nothing unusual about her labor or puerperium, other than the fact that she had a breech presentation.

Six weeks after confinement she was obliged to stop nursing the baby because of a breast abscess, and shortly after that she had a normal menstruation, sufficient proof of the presence and function of the remaining ovarian tissue.

Bimanual examination now shows a normal anteposed uterus, which is freely movable, and no evidence of further pathology in either lateral fornix.

Here, then, is a case where a laparotomy was performed in the twelfth week of gestation with operative manipulation of both ovaries, each of which contained dermoid cysts. The tumors, the entire right ovary, including beyond doubt the true corpus luteum, and a major portion of the left ovary were removed without untoward effects on mother or child. It is interesting to speculate what would have happened had one step further been carried out and the patient been deprived of all ovarian tissues. The amount and kind of ovarian tissue removed during pregnancy and the consequent effect upon the continuation of this process appears to be an extremely variable quantity, as many patients have aborted after laparotomy where much less work was done.

The records of the Woman's Hospital, covering, roughly, the last fifteen thousand admissions, show only eight patients who were operated upon during pregnancy with the express purpose of removing ovarian tumors and allowing pregnancy to continue. Of the other six all were operated upon between the twelfth and sixteenth week, the tumors having been discovered during routine examination when the patients presented themselves for diagnosis of pregnancy. In five of the six cases the pathologists found lutein cells in the material examined, and four of these patients aborted while still in the hospital. The fifth patient of this group, a colored woman of twenty-five, was still pregnant two months after her operation, and it is assumed that she went on to term. The sixth patient had a simple multilocular cyst, in which the

presence of lutein tissue was not mentioned, and she went on to term and a normal delivery. Two others with unilateral involvement were followed by normal pregnancy and confinement, one (1) of these being a simple and the other (2) a corpus luteum cyst.

DISCUSSION

DR. ROBERT T. FRANK.—In deciding on the clinical aspects of operating on ovarian tumors during pregnancy, three factors must be considered. In the first place, is the corpus luteum essential for the continuation of pregnancy, and if so, for how long a period is it essential? In the second place, is ovarian tissue, aside from the corpus luteum, essential, and if so, when? In the third place, we have to consider the mechanical tolerance of the uterus itself.

As far as the corpus luteum is concerned, we know that in different species it is essential for nidation for different periods of time. The earliest case in which nidation has proceeded after removal of the corpus luteum in which we have any really worth-while record is one between the fifth and sixth week of pregnancy. From then on I don't think that the removal of the corpus luteum plays any further rôle as far as nidation is concerned. I might add that, as a matter of fact, my work has convinced me that the placenta takes up the necessary hormonal secretion which is required to keep up the hyperplasia of the uterus in order that it may grow and form a proper container for the uterus.

As far as the mechanical tolerance of the uterus is concerned, I think the optimum time is between the fourth and seventh month. If during operation care be taken not to expose the uterus to the cold, to tie the pedicle as far away from the uterus as possible, to have as little intraperitoneal manipulation as is consistent with technical safety. I recall a case where I had to operate on a myoma which had become necrotic, in which I actually saw the fetus through the membranes. Unfortunately, I tore through the mucosa. I sewed it up carefully. That was about at four and a half months, and I later delivered the baby. That is about the most radical intervention that I know the uterus tolerates. On the other hand, I recall another woman who at the age of 21 had one ovary removed and then some two years later conceived, and at the fifth month a large abdominal tumor was found. The diagnosis lay between large hydroureter and ovarian cyst. We decided on ovarian cyst and I removed the ovarian cyst and the pregnancy came to term, which would be another case for Dr. Hurd to add to his statistics where the pregnancy came to term, in spite of the fact that no ovarian tissue existed. She never menstruated again, so that was pretty good proof that no ovarian tissue was left.

DR. E. H. DENNEN.—I have observed three cases of this nature, all in primiparae, one at six months, one at four and one-half months and the other at six to eight weeks. Two of them have since been delivered, one by low forceps, and the other normally. The third case, at six to eight weeks, is still in the prenatal clinic at the Nursery and Child's Hospital. One of the three cysts contained, according to the pathologist, a corpus luteum of pregnancy.

DR. EDWIN W. HOLLADAY.—Within the past few weeks I had a patient a little over three months' pregnant, whom I operated upon and the pathologist reported a corpus luteum cyst. The other ovary was carefully examined and there was no evidence whatever of any corpus luteum. She was well morphinized and given hypodermic of luetin for the first few days and then by mouth. She went on to term without any trouble whatever.

DR. LOUIS J. LADIN.—It has been my custom to operate for ovarian cyst, if it was sufficiently large to be palpated, in the early weeks or months of pregnancy. It

may be that I happened to have fortunate cases. This year I have had three. In one an ovary containing the corpus luteum was removed and the woman was recently delivered In another, subsequently delivered, there was a small dermoid cyst and a bad ovary containing a corpus luteum. Neither of these patients received luetin and it is not my practice to give it.

DR. MEYER R. ROBINSON read a paper entitled **An Orientation of the Biomechanism, Pathology and Clinical Phenomena of Extrauterine Pregnancy, Based on a Study of 131 Cases.** (For original article see page 1.)

DISCUSSION

DR. ALFRED PLAUT.—I would like to ask in what percentage of these cases the decidual reaction was timed. Without having data at hand, in the cases which I have had the opportunity of studying, I found between 5 and 10 per cent. This depends absolutely upon the frequency of the decidual reaction and leads to another point where disagreement of opinion must exist between different observers. I would never call this formation which partly or completely separates the sac from the tube lumen a reflexa because I consider the mechanism in the uterine nidation is a tubal nidation fundamentally different. In the uterine nidation the ovum is imbedded wholly in the so-called compact layer, giving a real, nearly compact layer of stroma cells and later on decidual cells which are situated between the surface of the epithelium and the areola of the glandular ducts. Such areola do not exist in the tube. A thick decidua giving a real bed for the ovum is very seldom, if ever, formed in the tube, so the ovum digs its bed in the other layers of the tube and so-called external rupture frequently follows. Secondly, in the uterus we have one lumen not interrupted by a solid structure. It lies behind the ovum when the latter has imbedded itself in the compact layer of the endometrium in the tube. On the other hand, there are the mucosal folds, the so-called villi, behind the ovum. A more or less inflammatory state is present in many, if not in all cases of tubal gestation; so the tubal folds may coalesce in a kind of membrane with a decidual reaction, and in some cases this results in a more or less complete separation of the ovum from the rest of the lumen. There is some resemblance between this layer and the reflexa, but, morphologically speaking, these two layers are different, and while it may be a matter of opinion, I, personally, would not call this layer a reflexa, putting it on equal footing with the reflexa in normal uterine pregnancy.

DR. EMILY D. BARRINGER.—I would like to ask what part gonorrhea plays in ectopic gestation.

In a series of 1300 cases of gonorrhea, diagnosed serologically and bacteriologically, we have not had one case of ectopic, and in the same series we had 71 cases of intrauterine pregnancy.

DR. LOUIS J. LADIN.—I am very glad that there are a few who still believe that the death of the ovum is not the cause of bleeding. Here is another instance where the clinical experience does not coincide with the laboratory experience. After watching and observing nearly 400 cases from the clinical standpoint, especially many years ago, when the main object in meeting a case of tubal pregnancy was to make the diagnosis, a great deal of study was given to the clinical features of the case. I do not hesitate to say that the absence of uterine bleeding in a case clinically, to me pointed to a termination of the pregnancy, and I do not care what the laboratory reason is for the same. Within recent years I have had occasion to prove that as soon as the uterine bleeding ceases there is no question that on opera-

tion, you will find a terminated pregnancy or an ovum that has been completely separated from its surroundings, whether it be in the tube or in the abdominal cavity.

As far as the question of tubal abortion is concerned, I agree with the reader of the paper that the term "tubal abortion" should not be applied to those instances where there is bleeding from either the fimbriated extremity or through a rupture, which I always have regarded as tubal abortion. With very few exceptions do tubal pregnancies go on to term; they abort.

DR. DAVID N. BARROWS.—I differ with the question of the usefulness of the tube after so-called tubal abortion. I treated a woman two years ago who was operated upon for tubal abortion and the tube left in. The other tube was removed a year or so later for ruptured tubal pregnancy and the woman subsequently had an intrauterine gestation, we believe, through the tube which was left in.

In a series of cases observed on the service at Bellevue, where we were watching for the "shoulder pain," it seemed to run somewhere between 33 and 40 per cent, and we did not consider it a very trustworthy sign.

Cullen's sign I have not observed as frequently, about four or five times in the last two years, and it seemed to have the color in those cases more of a hematoma or trauma, as for example, that of a "black eye," rather than the shimmer of blood through the skin.

DR. MEYER R. ROBINSON (closing).—I agree with Dr. Plaut that the histologic condition in the tube is different from that of the uterus. If they were similar the tubes would not rupture. I only laid stress on the fact that the moment the ovum is right for placentation, no matter whether it be in the uterine mucosa, the tubal mucosa, the follicular mucosa or the peritoneal surface, it does not remain on the surface, but digs its way into the submucous structures. In the uterus it needs a very hypertrophic, hyperplastic, highly vascularized layer, and that suffices for forming the future nest without invading the muscularis uteri, but when it gets into the tube and the tubal mucosa is not sufficient, it must encroach upon the tubal muscularis which only temporarily delays the final fatal termination, but does not prevent it.

As far as the lining of the tube and that of the uterus are concerned, they are microscopically different, but if we trace them back embryologically it is only a continuation of the same *anlage*. The uterus and the tube only later become differentiated. So whether Dr. Plaut wants to recognize the folding over of the tubal folds as being identical with the folding over of the mucous folds and call it a reflexa, is immaterial, but anatomically they are alike and they act similarly. Placental blood may escape; otherwise there would not be established an intercommunication between the maternal and the fetal structures. Physiologically they aim at the same thing and anatomically they don't differ very much. So we cannot help, at least in those cases where we find a reflexa, stating that it is a reflexa, even if it is an ectopic pregnancy.

The percentage of decidual reactions I cannot state, but my expeirence has been that the earlier in the course of pregnancy you examine ectopic pregnancy, the more likely you are to find a decidual reaction, and as the pregnancy grows older the finer structures of the decidual reaction are lost.

Dr. Barringer's information is very valuable, and bears out just what I stated in my paper, that it is not inflammation and it is not a purely mechanical condition, on which so much stress has been laid and repeated over and over again, which is the cause of tubal pregnancy. There is a far greater functional disturbance of the tube which is responsible in the vast majority of cases, in my experience, because real inflammatory conditions were not found frequently. Most of my cases showed no perisalpingitis, adhesions, torsions, twists or anything else; the tubes were per-

fectly normal. We had two only this afternoon and both had normal tubes—no gonorrhea or infection, and both women had borne children, one of whom had her last child about sixteen months ago and the other two years ago.

As to the question of leaving the tube: this also is included in my paper, but I did not read it. The question of leaving the tube behind was recently revived in Italy because one case is quoted where the tube was removed for a tubal pregnancy and the patient conceived again, resulting again in tubal pregnancy, and she had no children; therefore, these Italian operators became conservative, they incised the tube, removed the ectopic, closed the tube and let it alone. I agree with leaving the tube behind if you can guarantee as to which tubal pregnancy will terminate in a mole and which will go on to fatal bleeding. If I could tell these things beforehand, I would not operate on these cases.

Dr. Ladin's teaching regarding uterine bleeding is valuable, but I can only define my thesis by physiologic and pathologic facts as they have been given to us within the past ten years. If other reasons for bringing out the other viewpoints are stronger, I will be glad to change my viewpoint.

Department of Reviews and Abstracts

Conducted by Hugo Ehrenfest, M.D., Associate Editor

Selected Abstracts

Diseases Complicating Pregnancy

Ivens: Five Specimens Illustrating Necrobiotic Changes in Fibroids Associated with Pregnancy. The Journal of Obstetrics and Gynaecology of the British Empire, 1922, xxix, 639.

Examination of five necrotic fibroids, three removed during pregnancy and two during the puerperium, revealed marked degeneration in both the muscle and connective tissue. In the early stages the muscle cells were swollen, shortened and showed pycnotic changes in the nuclei. The general appearance resembled coagulation necrosis rather than hyaline degeneration. When degeneration was advanced, the whole fibroid was practically a homogeneous mass destitute of nuclei. Edema was not noted. Thrombi were not seen in the vessels. The line of demarcation between the normal uterine muscle and the fibroid tissue was sharp. Extravasation of blood occurred but was never accompanied by deposits of blood pigment. Leucocytic infiltration was sometimes present. The degeneration present in these tumors is due either to thrombosis or to a toxin acting only on the neoplastic cells.

H. W. Shutter.

Rioux: Necrotic Fibromata and Pregnancy. The Journal de Médecine de Bordeaux, 1923, xcv, 156.

The author found in the literature 28 cases treated by operative procedure with three resulting deaths. Excepting in interstitial tumors, severe pain was a symptom in all cases and developed with the cause for necrosis (torsion, pressure etc.). Nausea, vomiting, rapid pulse, temperature, jaundice, intestinal obstruction, distention and tension of the abdominal wall are symptoms which vary in intensity with the peritoneal involvement. Urinary disturbances are frequent. Examination usually reveals a painful periuterine tumor which may be found to have increased markedly in size with the onset of symptoms. Diagnosis is frequently difficult, the condition being confused with pregnancy in an incarcerated retroverted uterus, torsion in the pedicle of an ovarian cyst, pregnancy in the uterine horn, or appendicitis. The diagnosis of a necrotic fibroid complicating pregnancy calls for immediate operation. The choice of operative procedure depends on the period of pregnancy, the location and size of the tumor, the presence of infection and the condition of the patient. Myomectomy, the operation of choice, is simple in cases with pedunculated fibroids, but more difficult in the interstitial tumors and in the tumors of the lower segment in advanced pregnancy. Infection contraindicates myomectomy. Where a hysterectomy is to be done it is preceded by cesarean section when the fetus is viable.

H. W. Shutter.

Fischmann, E. W.: Fibroids in the Puerperium. Surgery, Gynecology and Obstetrics, 1924, xxxix, 327.

The author reports an instance in which a definitely palpated interstitial fibroid was spontaneously separated from its uterine wall attachments in the puerperium and subsequently partially expelled. After a critical review of the literature and

a survey of his own statistics, he concludes: (1) Fibroid tumors in the puerperium may cause serious complications, frequently a febrile course. (2) Fibroid tumors themselves may suffer changes during gestation and labor, and these may progress and even be augmented by secondary infection during the puerperium. (3) When a woman with a fibromyomatous uterus becomes pregnant and goes to term, cesarean section with an immediate myomectomy or hysterectomy is the operation of choice. (4) When the myoma is not discovered until during labor or in the puerperium, conservatism should be practiced as long as possible. WM. C. HENSKE.

De Gaudino, Maria Teresa F.: Ovarian Tumors Complicating Pregnancy, Labor, and the Puerperium. Semana médica, Buenos Aires, 1921, xxviii, 389.

Ten instances of this complication are reported occurring in 13,313 deliveries. Two of these were at term, and were explored by the abdominal route. In both cases, it was impossible to expose the tumor sufficiently without drawing the uterus forward in such a way as to endanger the blood supply to the placental site; consequently a cesarean section was necessary in each case. In the third case the diagnosis of a cyst was made during labor and it was punctured through the vagina. Cases 4 and 5 were cysts removed by laparotomy during the fifth and six months. The sixth patient left the clinic before labor. Case 7 was that of a patient with a cyst which ruptured during labor; a laparotomy was done the second day postpartum and drainage established, but the patient died of peritonitis. The eighth case was operated on two months after delivery, the tumors having been mistaken for inflammatory masses. The ninth and tenth cases were of tumors removed during the puerperium, the former for a twisted pedicle, the latter for malignancy.

Ovarian tumors diagnosed during the first months of pregnancy should be removed. In the last months those tumors localized in the abdomen and not interfering with labor should be let alone until after the puerperium. Pelvic ovarian tumors which cause dystocia should be removed during labor, without cesarean section whenever possible. During the puerperium such patients should be treated according to the symptoms caused by the tumor. THOS. R. GOETHALS.

Hermans: Acute Appendicitis during Pregnancy, Labor, and the Puerperium. Nederlandsch Tijdschrift voor Geneeskunde, 1924, ii, 1004.

Hermans does not believe that pregnancy is a predisposing factor of any great consequence, but does not doubt that a latent or chonic appendicitis may be activated by pregnancy. He reviews the literature and his own cases and comes to the following conclusions:

Appendicitis may complicate pregnancy at any stage, even during delivery. As a rule, the diagnosis during pregnancy, labor, and the puerperium is not especially difficult, the main point being to bear in mind the possibility of its occurrence. Only by prompt operation can the prognosis be improved, the earlier the diagnosis and operation, the better for mother and child. He agrees with Cooke: "In case of doubt operation is safer than waiting."

R. E. WOBUS.

Tédenat: Appendicitis Among Pregnant Women. Bulletin de la Société d'obstétrique et de Gynécologie, 1925, xiv, 237.

In the French literature there is a marked paucity of information regarding appendicitis during pregnancy and the puerperium. In the Baudelocque Hospital in Paris, among 11,479 labors during a period of six years, there was only one case of appendicitis.

Since the prognosis is doubtful, all cases of acute appendicitis should be operated upon as soon as the diagnosis is made. During pregnancy the tender point is higher than McBurney's point and often there is an area of inflammatory edema near the costal margin and even in the flank in cases of retrocecal appendicitis. In three cases operated upon by the author, recovery was uneventful. The patients went to term and had spontaneous labors and normal puerperia. In a fourth case the operation was difficult because of a purulent retrocecal fistulous tract which had to be drained. There was much shock, and the patient aborted six days after the operation. In a fifth case operation revealed pus in the right side of the abdomen all the way up to the diaphragm. Metastatic arthritis of the knee occurred and the patient died of sepsis on the tenth day. J. P. GREENHILL.

Stork, F.: Pregnancy and Ileus. Monatsschrift für Geburtshilfe und Gynäkologie, 1925, lxix, 12.

To the 128 cases of ileus occurring during pregnancy which had been reported in the literature, Stork adds five cases. Laparotomy was performed on all five patients, but one died. The latter had an invagination of the small intestine. In four of the cases an abdominal cesarean section was performed at the time of treating the ileus, while in the fifth case a vaginal cesarean section was done. In the four cases with abdominal cesarean, the baby was delivered before the ileus was corrected. In the future the author says the first step will be laparotomy and the decision to empty the uterus will depend upon the individual case. At the end of pregnancy and wherever there is a viable child, a cesarean section is indicated at the time of the laparotomy; for aside from the fact that the gravid uterus inhibits peristalsis, many fetuses die from toxins liberated during the period of intestinal obstruction and two-thirds to three-quarters of the fetuses that do not succumb, are expelled prematurely. Such uterine activity may be harmful to a patient recently operated upon. J. P. GREENHILL.

Moeller, W.: Mechanical Ileus during the Puerperium. Monatsschrift für Geburtshilfe und Gynäkologie, 1922, lix, 273.

The author reports the case of a woman who suddenly developed acute abdominal symptoms during the puerperium. At operation a mechanical ileus was found which was due to a band extending from the flexura sigmoidalis to the right inguinal region.

Repeated pregnancies and labors greatly diminish the likelihood of mechanical ileus. Statistics of all cases of mechanical ileus occurring between the ages of fifteen and fifty, show almost twice as many in men, whereas the numbers were approximately the same in both sexes after fifty years of age. This is noteworthy, as women have as many inflammatory conditions of the abdomen as men and have much more often gall bladder disturbances. They also have a great deal of genital pathology and numerous gynecologic operations, all of which tend to produce adhesions which may give rise to mechanical ileus. Of the 12 female patients who had ileus, no less than 7 had never been pregnant. Of the remainder there was an interval of from three to seventeen years between the last labor and the occurrence of the ileus. J. P. GREENHILL.

Schoeffer and Keller: Torsion of the Omentum during Pregnancy. Bulletin de la Société d'obstétrique et de gynécologie de Paris, 1923, xii, 441.

Torsion of the large omentum is very rare, only 134 cases having been reported up to 1913. From experimental work on animals as well as from clinical experience it has been shown that the chief factor in the production of this torsion is the for-

mation of a pedunculated mass of omental tissue, while in others it is the fixation of the free end of the omentum to the bottom of a hernial sac or to any point of the abdominal wall. The weight of the mass which tends to lengthen the pedicle more and more, plays a greater rôle than the increase in venous pressure in the pedicle and the unequal growth of the mass. The immediate causes of torsion are mechanical in nature, as for example, peristaltic movement or strong abdominal pressure.

The symptoms of torsion without a hernia are usually vague at the beginning, but later there are acute symptoms which tend to confuse the condition with appendicitis. The crisis itself begins abruptly in a healthy person in the form of an acute pain in the right iliac fossa. Peritoneal symptoms predominate. There is vomiting, no passage of feces or gas, abdominal distention and the peritoneal facies. Soon, however, the symptoms disappear and one can feel a tumor mass at the site of pain.

The author reports the case of a primipara who had an attack of pain in the fifth month of pregnancy. A diagnosis of appendicitis or subacute cholecystitis was made, but at operation a twisted omentum was found. The twisted mass was resected. No similar case has been reported in the literature. J. P. GREENHILL.

Merletti, D. C.: Spasmophilia and Pregnancy. Annali di ostetricia e ginecologia, 1925, xlvii, 247.

In this article various conditions which often occur in pregnancy are considered in their similarity to comparable manifestations of spasmophilia. While laryngospasm is rare in pregnancy, spasm of the pharynx and esophagus are not uncommon, especially in nervous hyperesthetic women in whom hyperexcitability can be determined by electrodiagnostic measures. Spastic mydriasis of the pupils is also frequent in nervous subjects; so also cardiac tetany, which gives rise to faintness and at times syncope, together with variations in the heart rate. Localized spasm of the antral portion of the stomach and of the pylorus has been found by radioscopy to coincide with the nausea of pregnancy, and to persist without antiperistalsis during the act of vomiting.

Eclamptic convulsions are considered by the author to be closely parallel to the infantile convulsions of spasmophilia. Alimentary factors are important in both conditions, and the season is also a factor, inasmuch as convulsions are more common in cold than in warm weather.

The author concludes that in certain women there exists a state of constitutional hyperexcitability of the nervous system, which may be measured by response to electric stimuli, and which induces a disposition to localized spastic conditions and to convulsions. This state he would call spasmophilia of pregnancy, and would attribute it to endocrine dysfunction with especial parathyroid insufficiency. The treatment includes administration of calcium, bromides, and parathyroid extract, and the use of the ultraviolet ray in addition to dietary and eliminative measures.

THOS. R. GOETHALS.

Lambrinudi: Maternal Birth Palsy. British Journal of Surgery, 1925, xii, 554.

While pressure symptoms, such as cramps and pain along the course of the sciatic nerve, are relatively common during the latter months of pregnancy, actual paralysis is rather a rare condition. Lambrinudi reports two cases which came under his observation. In the first case, a primipara thirty years old, was delivered by high forceps after fourteen hours of labor. When she came out of the anesthetic, she experienced numbness and weakness of the entire right lower limb. On getting up three weeks later, she noticed acute pain along the back of the thigh and outer part of the leg and foot. There was definite foot drop. Five months later, she still showed paralysis of the toe extensors, the tibialis anticus and the pernei, with some

weakness of the toe flexors. Under treatment recovery progressed slowly. In the second case, a woman had lost her first child during labor three years previously. While supposed to have a flat pelvis, she delivered spontaneously a seven and a half pound baby after seventeen hours' labor. During the second half of the labor, she noticed acute cramps in the right leg below the knee. She felt relief afterwards, but a feeling of weakness and numbness persisted. On getting up, she noticed a right foot drop. There was definite paresis of the muscles supplied by the right external popliteal nerve, with dullness of sensation over the same area. The loss of sensation returned after two weeks, but the paresis remained. The author also quotes a case reported by Patel, in which the paresis came on spontaneously when the patient was five and a half months pregnant.

Lambrinudi discusses the theories advanced, especially toxic neuritis and pressure on the sacral roots, but believes it is due rather to traction on the sacral cord caused by a rotation of the sacrum. For this reason he condemns the practice of flexing forcibly the woman's thigh on her abdomen during delivery. In support of his contention, he quotes Fleming who states that the condition is not rare in the cow, in which it occurs usually from six to twenty days before labor. In making post-mortem examinations in such animals the gluteal muscles were found to be infiltrated and some of its fibers ruptured. The sacral cord showed evidence of injury ranging from the finding of large amounts of free fluid in the spinal canal with congestion of the membranes to the finding of actual injury to the cord with the presence of blood clots.

R. E. WOBUS.

Bourne: Etiology and Prognosis of Puerperal Insanity. Journal of Obstetrics and Gynaecology of the British Empire, 1924, xxxi, 251.

In the majority of cases the author found sufficient cause for the production of insanity even in the absence of any tendency toward the disease. In only 9 out of 69 cases could no cause for the disease be found. Eighteen had records of previous mental trouble or a bad family history. Infections after delivery accounted for eighteen (27 per cent) of cases. Nine suffered from eclampsia and 8 had had difficult labors. Anxiety during pregnancy seems a factor in the disease as 36 per cent of the mothers were unmarried.

Four women developed symptoms during pregnancy, 6 during labor, 39 in the first week of the puerperium, and 18 in the second week. The usual onset of the condition was sleeplessness after which anxiety and incoherent speech were common symptoms. Most cases were maniacal by the third day, a few were depressed and stuporous. Thirteen patients died, 6 of sepsis, 2 of self-destruction, and 2 of cardiac failure. Of 36 patients surviving 78 per cent were discharged as recovered, 4 as improved. All cases associated with uterine infections recovered in from a few weeks to eighteen months. Where eclampsia was a factor recovery was rapid. The average recovery time for the series was six and one-half months. If insanity is associated with serious organic disease, such as sepsis or eclampsia, the prognosis is good and recurrence infrequent. In the presence of previous attacks or a bad family history the outlook is less favorable.

H. W. SHUTTER.

Nevermann: Narcolepsy during Pregnancy. Deutsche medizinische Wochenschrift, 1921, xlvii, 1164.

A case of this rather rare disease is recorded, occurring in a primipara, twenty-seven years of age. During the twenty-sixth week of pregnancy, the patient was unable to sleep for three days and nights. After this, she was constantly overcome by sleep during the day, although she slept quite well at night. She would go to sleep during a conversation, at her work, or while walking, and then would be awak-

ened by stepping from the sidewalk, by striking against a tree, etc. Examination by a neurologist revealed no neuropathy, nor was it possible to determine any other pathologic process. Treatment of various sorts was of no avail, however, the condition subsided spontaneously at about the thirty-second week of her gestation. Later she was delivered of a normal child. R. E. WOBUS.

Silberstein: Raynaud's Disease and Pregnancy. Zeitschrift für Geburtshülfe und Gynäkologie, 1921, lxxxiv, 208.

The author sketches briefly the chief clinical features of the disease, including the three types of attack: local syncope, local asphyxia, and gangrene. The patients are usually young neurotic women with a certain ability of the vasomotor system and the attacks frequently follow exposure to cold or psychic trauma. Other etiologic factors are intoxication and infections. Pregnancy seems to increase the severity of the disease, though there are but few reported cases. The author reviews these briefly and reports in considerable detail his own case which occurred in a neurotic young primigravida of twenty-two years. An attack of influenza in the third month was followed by an acute glomerulonephritis and three distinct Raynaud attacks, the second resulting in gangrene of several finger and toe tips. One attack followed prolonged exposure of the hands to cold water, another a family quarrel. Improvement was distinct and rapid following the induction of premature labor, which was indicated by the advancing nephritis and the severe secondary anemia. The author believes that pregnancy may aggravate the disease. Abortion is indicated in cases where gangrene is feared and its possible results are not offset by the desire for a living child. Where gangrene has already occurred, the indication no longer exists, since recurrence of attacks of gangrene is exceedingly rare. Especially in the pregnant cases, ergot poisoning must be considered in the differential diagnosis. MARGARET SCHULZE.

Hussey, P.: Mental Conditions and Pregnancy. Revue Suisse de Médecine, 1922, xxii, 473.

The frequency of psychoses of pregnancy is difficult to determine, figures varying widely from 0.2 to over 1 per cent. Of these about 15 per cent occur during pregnancy, the rest in the puerperium. Toxic conditions, infections, and idiopathic conditions all appear to have a part. These mental complexes have no definite type peculiar to pregnancy, but the melancholic and depressive types play by far the larger rôle. This last class is to be divided into two separate groups, the maniac depressive type with fairly clear-cut symptoms, and the other class a psychopathic syndrome in the particular individual. In this group we find that fear of death in labor or a dread of what may occur cause the depression, and even may force the patient to think of suicide. Schizophrenic, hysterical, apathetic, and catatonic conditions may occur. The majority of the conditions come during the period of lactation and in the early puerperium. All these conditions need careful observation and study. If the condition cannot be benefited by the proper therapy then abortion is the choice. Some cases in which paralyses, catatonic conditions, suicidal attempts have been observed demand not only abortion but also sterilization, and of course this holds true where a definite neurologic disease is diagnosed with a grave prognosis. A. C. WILLIAMSON.

Maclean: Notes on Three Cases of Chorea Gravidarum. Journal of Obstetrics and Gynaecology of the British Empire, 1922, xxix, 630.

From the frequent history of previous attacks of chorea and articular rheumatism, the associated endocarditis and the resemblance of the condition to Sydenham's chorea, one must continue to classify chorea gravidarum as an infection and not as

a toxemia of pregnancy. The onset of symptoms is usually in the first three months and it generally occurs only in primigravidae. The mild cases recover and only exceptionally bring about spontaneous abortion. Mild cases respond to isolation, diet (milk) and such drugs as arsenic, aspirin, bromides, and chloral. The severe types carry a mortality of 20 to 30 per cent. Drug treatment is ineffective in the latter. The patients are hard to nourish and grow progressively weaker. The mortality is formidable with or without the interruption of pregnancy, but statistics justify the induction of premature labor if done before the onset of exhaustion.

H. W. SHUTTER.

Ahlbeck: Polyneuritis Gravidarum. Archiv fuer Gynaekologie, 1922, cxvii, 41.

Ahlbeck reports seven cases of polyneuritis gravidarum of which 4 were in primiparae. All began during the first eight weeks of pregnancy with the pernicious form of vomiting; four became icteric. Psychoses set in with dullness, loss of interest, and loss of memory; one had severe headache; two suffered from hallucinations, and one had retinal hemorrhages. Therapeutic abortions were immediately done in all of the cases but the peripheral nerves were already involved in six. Numbness and muscular atrophy persisted for some months. Examination twelve to eighteen months later showed all to have recovered normal gaits, but six still suffered from impaired memories.

RALPH A. REIS.

Elkin: Spontaneous Labor in a Case of Decentralized Uterus. Journal American Medical Association, 1922, lxxiii, 27.

A woman of thirty-five years suffered from cervical Pott's disease with an almost complete transverse lesion at the seventh cervical segment. She became pregnant and, at term, went into spontaneous labor. She experienced slight pain during the second stage, but there were no abdominal contractions, the uterus emptying itself after a labor of two hours' duration. The position was occipitoposterior and the child, which appeared perfectly healthy in every way, weighed six pounds. The mother died on the ninth day postpartum from tuberculous pneumonia.

R. E. WOBUS.

Nishizuka and Iijima: Relations between Acute Infectious Diseases and Pregnancy. Kinki Fujinkwa Gakkwai Zassi, 1925, viii, No. 2, 7.

In 67 patients with typhoid fever, spontaneous abortion occurred mostly in the second and third week of the disease in 58.2 per cent, with a maternal mortality of 35.9 per cent, which was about twice as large as the mortality in the cases in which pregnancy progressed undisturbed by the intercurrent disease.

In 11 cases of paratyphus the percentage of spontaneous interruption of pregnancy was only 22.2 per cent, the maternal mortality also being decidedly lower than in typhoid.

In 54 cases of dysentery during pregnancy, spontaneous interruption, generally occurring in the second and third week of disease, amounted to 33.3 per cent with a maternal mortality of 44.4 per cent, which is even higher than in typhoid. In all of these three types of infections it was observed that as a rule the patients with high temperatures miscarried, while miscarriage only rarely occurred when the fever ranged low. These observations seem clearly to indicate that the artificial interruption of pregnancy as a therapeutic measure will only tend to increase the risks to the mother.

There were too few cases of cholera, scarlet fever, smallpox, influenza and diphtheria in this series to permit valuable deductions.

AUTHOR'S ABSTRACT.

Unger, R.: Successful Treatment of Severe Progressive Paralysis during Pregnancy with Malarial Inoculations. Medizinische Klinik, 1925, xxi, 1498.

The association of pregnancy and progressive paralysis is uncommon. At the Rudolph-Virchow Hospital two cases were seen within six months. Both patients were in dire distress on admission and both showed the bad effect of pregnancy on the paralysis. Unger reports in detail the case of a patient who was treated for paralysis during pregnancy by means of inoculation with the quotidian type of malaria. The patient's husband had previously been successfully treated for general paresis by means of malarial inoculations.

The patient who was admitted in a critical condition, had 22 febrile elevations as high as 102.2° F. during the course of the treatment. At term she had an almost painless labor and delivered spontaneously a living child which weighed 2640 grams. The child was normal in every respect. Its Wassermann test was negative in contradistinction to the mother who had a strongly positive Wassermann reaction, and its blood like that of the mother showed no malarial organisms. The puerperal period was uneventful and the patient left the hospital with her baby on the thirteenth day.

The case shows that an intensive malarial cure did not endanger the pregnancy. The high temperature and chills did not cause an abortion, although other febrile conditions often do cause the termination of pregnancy.

Two months after the malaria fever disappeared, which occurred spontaneously, there was begun a course of treatments with neosalvarsan. J. P. GREENHILL.

Deromps: Malaria and Pregnancy. Bulletin de la Société d'obstétrique et de gynécologie, 1924, xiii, 227.

Physicians fear to prescribe for pregnant women suffering from malaria the necessary dose of quinine. Even those who are convinced of the innocuousness of treating malaria in pregnant women intensively, do not dare to prescribe full doses because of the fear of being held responsible for an abortion or premature labor if these should occur during the course of treatment.

Clinical observations, however, leave no doubt of the absolute necessity of administering quinine intensively. Malaria in pregnant women is much more progressive than in nonpregnant; the disease kills fetuses, produces abortion and may be transmitted to the fetus. Quinine seems to affect the uterine musculature only during labor but does not stimulate contractions as long as the cervix is closed.

It is true that only about 18 per cent of women with malaria go to term and this is probably the reason why abortion and premature labor are often attributed to the administered quinine. In these cases, however, the interruption of pregnancy is rather due to the fact that quinine is employed in a dosage insufficient to prevent the abortion. Pregnancy is interrupted because of the febrile reaction, and also as a result of the death of the fetus. Pregnancy at times affects the malaria patient to such an extent that a marked anemia results which may be fatal. Some patients who had malaria long before they became pregnant and had no recurrence during pregnancy have a return a few hours after labor especially if the latter had been associated with trauma. Such cases might be confused with puerperal sepsis.

J. P. GREENHILL.

Puigy Roig, Pierre: A Case of Fetal Smallpox together with Maternal Smallpox. Gynécologie et Obstétrique, 1922, vi, 176.

The author reports in some detail a case of fetal smallpox acquired from the mother leading to intrauterine death of the fetus. This occurred about the fifth month of gestation. The fetus was mummified and presented typical pustules of variola. F. L. ADAIR.

Regan-Litvak-Regan: Intrauterine Transmission of Anthrax. Journal American Medical Association, 1923, lxxx, 1769.

These authors take up the literature dealing with experimental work and case reports and add a complete report of the fifth case on record. They were able to show conclusively that the anthrax bacillus was capable of passing through the human placenta. The mother died of anthrax during the fifth or sixth month of pregnancy. The fetus was removed by section and all smears made from its various organs and the placenta showed the anthrax bacillus. W. KERWIN.

Koerting: The Treatment of Influenza in Pregnant Women. Therapeutische Halbmonatshefte, 1921, xxxv, 655.

Statistics from the Prag clinic show a higher incidence of influenza among the female attendants than among the waiting pregnant women; the mortality, however, is far higher in the latter. This indicates that pregnancy does not predispose to influenza, but does exert an unfavorable influence upon its course and especially is this true in the latter months of pregnancy. This is explained partly by a diminished resistance of the pregnant woman to toxic influences, but more by mechanical factors, since in advanced pregnancy the respiratory excursion is diminished and increased work is thrown on the heart and the circulatory system.

The mild cases need little more than rest in bed, salicylates, and diaphoresis. The multiplicity of therapeutic agents recommended in the severe cases indicates that none are entirely satisfactory. In the severe cases with profuse serous exudate in which the patients literally drown in their own secretions, the author has had good results with the use of adrenalin.

Abortion in cases of influenza in early pregnancy is not indicated, since the mechanical factors do not come into play. Later, emptying the uterus might have a beneficial effect, yet this is overbalanced by the trauma incident to the labor. Many of these cases fall spontaneously into labor, and these should be spared during the second stage by delivery with forceps. Major operative procedures usually give bad results. Postmortem cesarean section should be done when indicated, but will usually fail to save the child. MARGARET SCHULZE.

Mosher: The Complication of Purpura with Gestation. Surgery, Gynecology and Obstetrics, 1923, xxxvi, 502.

Mosher was able to find only 39 cases of purpura complicating pregnancy in the literature, to which he adds a case of his own. The condition has been observed mostly in multiparae and manifests itself ordinarily in the latter months of pregnancy. It is usually of the hemorrhagic form and characterized by hemorrhages from the mucous membranes, petechiae and ecchymoses, nonretractile blood clot with normal coagulation time, and a tendency to metrorrhagia. The diminished number of blood platelets is the most constant finding and is supposed to be the direct cause of the condition. Frequently other pathologic complications of pregnancy such as toxemia and infection are present and may be the cause of the purpura, but rarely the purpura is the only pathologic state demonstrable. Abortion or premature delivery is the rule, and influences the outcome favorably.

The child may or may not be affected, yet only one-half of the fetuses survive. The mother usually dies at, or soon after, labor from hemorrhage, if she carries her child to term.

Blood transfusion is the only remedy of any value, but must be repeated frequently as the platelets which are thus introduced are soon destroyed.

R. E. WOBUS.

Insfran, Jose V.: Treatment of Hookworm Disease in Pregnant Women with Carbon Tetrachloride. Journal of American Medical Association, 1926, lxxxvi, 735.

Previous to the introduction of carbon tetrachloride as treatment for hookworm disease, pregnancy was considered as a contraindication for antihelmintic medication. The writer treated more than a hundred thousand of the population of Paraguay with a combination of carbon tetrachloride and oil of chenopodium. All pregnant women were treated with carbon tetrachloride alone in a dosage of 2.4 c.c. with a simultaneous purge of magnesium sulphate. Two hundred and nineteen pregnant women could be followed until after delivery; in this group five abortions occurred.

GROVER LIESE.

Rio, L.: Tobacco Intoxication in Pregnancy. Annali di Ostetricia e Ginecologia, 1925, xlvii, 266.

The effects of tobacco upon cigar workers have been variously interpreted, and reports of investigators have been conflicting.

To determine the effect of such absorption upon fertility and pregnancy the author made use of guinea pigs, subjecting them to measured doses of extracts of tobacco leaves mixed with their food. In the first series, animals were subjected to intoxication before and during mating, in a second series, pigs were so treated after conception. Each series is subdivided into two groups, one subjected to mild doses, the other severely intoxicated. Series I, Group I, became pregnant and remained so; Series II, Group I showed a normal course of pregnancy, and were delivered at term of normal fetuses which were fully developed and which lived. Series I, Group II remained sterile, while in Series II, Group II, pregnancy was with one exception interrupted, with all fetuses stillborn or nonviable.

The author does not believe that the lowered fertility of Series I, Group II, is due to alterations produced by tobacco on the generative organs, for the uterus and ovaries in all these cases showed no variation from normal. In both Group II, however, the animals showed marked cachexia and loss of weight, and to this the author attributes both sterility in Series I and the birth of dead or nonviable fetuses in Series II.

THOS. R. GOETHALS.

Favreaux: The Thyroid Function and Pregnancy. Journal de Médecine de Bordeaux, 1922, xciv, 87.

During pregnancy there is a reciprocal action between the elements of the endocrine system which unites them in maintaining equilibrium and providing a physical defense against the toxic products of conception. The thyroid exerts a definite influence on the development and functions of the reproductive system through its effect on ovulation, menstruation, gestation, and lactation. Pregnancy and lactation call forth an increased thyroid activity shown in the gland by hypertrophy and a numerical increase in follicular elements. In certain cases this hyperactivity becomes pathologic and may persist. At the onset of pregnancy a certain amount of parathyroid insufficiency is seen. Hypothyroidism, a compensatory hyperthyroidism and a persistent, absolute hyperthyroidism have followed successively in the same patient. Pregnancy may be diagnosed in some animals, for example the cat, by the thyroid hypertrophy.

Where absolute hypothyroidism or myxedema exists, sterility is the rule. Fecundity in the hypothyroid cases seem to vary in direct proportion to the amount of gland tissue still functioning. When pregnancy exists these women usually go to term with about the normal percentage of complications, albuminuria, etc. When the woman with a previous total thyroidectomy becomes pregnant, tetany, albuminuria and mental and trophic disturbances are the rule. Partial thyroidectomy fol-

lowed by partial loss of parathyroid function predisposes to tetany in pregnancy. Aggravation of the condition during pregnancy is the rule in milder myxedematous cases, however, regression usually follows normally after term. Mild hypothyroidism is frequently benefited and occasionally cured by the compensatory thyroid activity of pregnancy. Except in pronounced myxedema, gland therapy during pregnancy gives good results. Apathy, hypothermy, sterility and even death are some of the sequelae supposed to have followed pregnancy in the partially thyroidectomized patient.

Sterility is the rule in the pronounced cases of hyperthyroidism. Toxemias and other complications exclusive of those arising in the thyroid are present in about the normal percentage in these patients. Predisposition to hemorrhage and hypertension have been noted in pregnancy complicated by hyperthyroidism. The symptoms of Graves-Basedow's syndrome are variously influenced by pregnancy. Lactation usually has a quieting influence on these women and nursing is generally indicated. Occasionally the milk in hyperthyroid mothers affects the offspring, even producing exophthalmos and tremor. Tetany, achondroplasia and varied disturbances of the osseous system have been noted in the nursing infants of mothers suffering from hyperthyroidism. H. W. SHUTTER.

Knaus: Thyroid Function during Pregnancy. Archiv fuer Gynaekologie, 1924, cxxiii, 26.

Knaus tested the thyroid function in 35 pregnant women in the last months of pregnancy by injecting 0.02 mg. of epinephrin intravenously and immediately following it by an injection of epinephrin subcutaneously. The results obtained and the data which he had gathered from previous investigations, together with the results obtained by other investigators, leads him to conclude that there is a hypofunction of the thyroid gland during pregnancy rather than a hyperfunction as has been previously taught. Four patients who died intrapartum showed, histologically, a hypofunctioning thyroid gland. He believes, therefore, that thyroid therapy is indicated in pregnancy edema and other allied conditions. RALPH A. REIS.

Jülich, W.: Basedow's Disease and Pregnancy. Medizinische Klinik, 1925, xxi, 928.

According to Novak and Seitz, among 98 cases of Basedow's disease associated with pregnancy that were reported in the literature, 60 per cent became worse while 40 per cent were not adversely affected. Some patients in fact improved during pregnancy. Jülich reports two cases of his own. In the first case, the patient near term had such severe subjective and objective difficulties that pregnancy had to be interrupted to save the patient's life. The second patient previously had an operation performed because of Basedow's disease and had practically no symptoms for four years. However, during pregnancy the thyreotoxicosis was so marked that the pregnancy had to be ended. In both patients examination later showed that subjective symptoms and objective signs had considerably diminished.

The author is of the opinion that a patient with Basedow's disease should avoid conception. J. P. GREENHILL.

Vignes, H.: Parathyroid Glands and Pregnancy. Journal de Médecine de Paris, 1925, xliv, 7.

Vignes finds that during pregnancy there occurs a certain amount of parathyroid hypertrophy, due to a cellular multiplication. During pregnancy the calcium metabolism of the body is, to a large extent, controlled by these glands. Though the exact mode of action is not known, a parathyroid insufficiency is associated with a decalci-

fication of the blood and tissues, which in turn lowers the sugar tolerance causing an abnormal excitability of the nervous system and tetany.

Intravenous injections of calcium lactate may relieve the symptoms temporarily, but permanent cure can be reached only by following successful parathyroid transplantation.

Vignes concludes that little is as yet known concerning the relation between the parathyroid gland and pregnancy. THEODORE W. ADAMS.

Metzger, E. L., Simon, M., and Wineberg, H.: Examination of the Field of Vision in Pregnant Women. Monatsschrift für Geburtshilfe und Gynäkologie, 1925, lxx, 140.

Fifty-six pregnant women were examined by the authors to determine whether the field of vision was changed in pregnancy. Despite recent claims to the contrary, the present authors could not find any diminution in the field which could be attributed to any disturbance in the region of the optic chiasm in a single patient. On the other hand, they did find functional deviations from the normal. The eyes during pregnancy readily show functional disturbances which remind one of the disturbances in hysteric and neurasthetic individuals. J. P. GREENHILL.

Klaften: Contribution to the Knowledge of Pregnancy in Hemeralopia. Zentralblatt für Gynäkologie, 1923, xxxii, 1288.

Klaften reports observations on some dozen cases of hemeralopia developing in pregnancy, apart from the cases of hemeralopics who became pregnant. These are two distinct entities, as the hemeralopia of pregnancy appears to be a temporary condition, wherein the course and prognosis differs entirely from ordinary hemeralopia. It appears shortly before the end of the pregnancy, is uneffected by treatment, and disappears spontaneously after confinement. Recurrence of the disease in several pregnancies, and the observation that nonpregnant women suffer relatively infrequently from this condition in the childbearing age, suggests pregnancy as a causative factor. The author has made many attempts to determine the etiology of the condition, whether associated with altered function of the kidneys, liver, or cardiovascular system, but was unable to find any cause of relationship between disease of any single organ and the hemeralopia. On the other hand, many normal patients were examined during pregnancy, as well as many others suffering from various toxemias, and no trace of the affection was discovered. Under ordinary circumstances menstruation, or the associated function of the ovary, seems to account for the lessened tendency to hemeralopia of women in the childbearing age, and the disappearance of menstruation during pregnancy seems to be one factor in its production. Apart from this it is probable that the associated complex of alteration of various organs during pregnancy is a factor, and that hemeralopia is a manifestation of pregnancy toxemia. LITTLE.

Schall, E.: On the Question of Bitemporal Hemianopsia in Pregnant Women. Monatsschrift für Geburtshilfe und Gynäkologie, 1925, lxviii, 75.

Recently Löhlein published a report in which claims were made that there is a pronounced bitemporal hemianopsia during the last month of pregnancy in 80 per cent of pregnant women. Schall examined 68 pregnant women to determine the validity of this claim, but he could not find a single woman who had hemianopsia. Schall attributes this difference to the fact that Löhlein's tests were carried out by an inexperienced man. Schall points out that for an hypophysis to produce pressure on the optic chiasm it must be large enough to produce changes in the sella turcica that can be recognized in a roentgen-ray plate. However, in pregnant women there is no enlargement of the sella turcica. J. P. GREENHILL.

Fruhinsholz, A.: Thyroparathyroid Insufficiency in Pregnancy. Gynécolgie et Obstétrique, 1922, vi, 145.

The author considers thyroid insufficiency in pregnancy under the headings: (1) athyroidism and, (2) hypothyroidism in pregnancy, (3) surgical hypothyroidism in pregnancy, (4) medical hypothyroidism. He considers (a) pregnancy with slight hypothyroid syndrome associated with migraine, chronic rheumatism and asthma; (b) pregnancy with marked myxedema. He reports a number of cases with detailed observations of these various conditions. He has a large group with parathyroid insufficiency in pregnancy in which he considers tetanus and eclampsia. The author draws no definite conclusions from his observations. F. L. ADAIR.

Jung: Clinical Course during Pregnancy of an Enlargement of the Hypophysis. Schweizerische Medizinische Wochenschrift, 1922, lii, 61.

The case reported is similar to that of Fehr in which a bitemporal hemianopsia had resulted, due to pressure on the optic nerve by the enlarged pituitary body. Although the visionary disturbance had persisted since the enlargement early in the second pregnancy and was now of ten years' standing, there was no acromegaly, glycosuria or polyuria. Jung's case is similar. The bitemporal hemianopsia having developed during a tenth pregnancy. At the close of the seventh month the x-ray showed definite enlargement of the pituitary, the visual disturbance was profound and the papilla whitened to some extent. Pregnancy was interrupted and the woman sterilized. In three days the patient was able to recognize persons in the room although the visual disturbance had not cleared up. The rapid subsidence of symptoms suggest a physiologic engorgement of the hypophysis due to pregnancy or a latent adenoma rather than a gumma or a malignant newgrowth.

A. C. WILLIAMSON.

Löhlein, W.: Bitemporal Hemianopsia in Pregnant Women. Monatsschrift für Geburtshilfe und Gynäkologie, 1924, lxv, 129.

The author examined the fields of vision in pregnant women every week during the last two months before labor and found during the last four weeks a constant and definite bitemporal diminution. The greatest limitation in 78 per cent of his subjects was found at the time of labor. The diminution first affected the colors, especially red and green. The change was observed more frequently among older women and this was due to the fact that most of the multiparas were found in this group. The number of births had a definite influence on this restriction of the visual field. All patients showed a definite improvement about the tenth day postpartum and in 80 per cent of the primiparas the fields had returned to normal at this time. In multiparas there remained a definite and permanent limitation.

This phenomenon is due to a physiologic hypertrophy of the hypophysis during pregnancy. The hypertrophy begins during the fourth month of gestation, and retrogression can be observed macroscopically one week postpartum. In repeated pregnancies there remains an increased number of chief cells which produce an intensive hypertrophy of the hypophysis in subsequent pregnancies. Very rarely is there such a degree of limitation in the field of vision that the patient notices it.

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